Disorders of Keratinization

(تقسيمة رووك)

1-Ichthyosis
2-Erythrokeratoderma
3-Porokeratosis
4-PPK
5-Acanthosis nigricans
6-Pityriasis rotunda
7-Peeling skin syndromes
8-Folliculocentric keratotic disorders
9-Pityriasis rubra pilaris
10-Darier's disease and related disorders(TAD and PAD)
11-Confluent and reticulate papillomatosis
12-Others.

Ichthyosis

Def: this form Comes from Greek Word "Ichthys = Fish"

Ichthyoses: group of (Genetic & Acquired disorders ch- By (Generalized, persistent, non-inflammatory scaling of skin.

- Classification:-

[A] Hereditary Ichthyoses:

AD

- Ichthyosis Vulgaris
- BCIE (Epidermolytic Ichthyosis (Hyperkeratosis)
- Ichthyosis bullosa of Siemens (IBS)
- Ichthyosis Hystrix (IH)
- Ichthyosis en Confetti: BCIE → Ichth. ē Confetti like Island of NL skin

AR

- (Lamellar Ichthyosis)
- NBCIE (CEI)
- Harlequin fetus or Ichthyosis

XLR

- X-linked Recessive Ichthyosis

[C] Ichthyosiform Syndromes: "10" (K 10)

- Refsum's
- Rud's
- CHILD*
- KID*
- Conradi Hunerman
- Chanarin Dorfman
- Netherton*
- Sjogren Larsson
- PIBIDs*
- Multiple sulfatase deficiency.

[D] Acquired Ichthyosis:-

[E] Related disorders:

- Ichthyosis linearis circumflexa.
- Ichthyosis Bullosa of Siemens
- Erythrokeratodermas
- Pit. Rotunda
- Skin Peeling Synds

Hereditary Icthyoses

1- Clinical picture

"2nd Most Common"

	Vulgaris (AD)	Lamellar (AR)	X- Linked (XLR) (♂ only)
	1 : 250	1 : 50,000	
Onset:	• Not at birth, Most at 1st Year & ± early childhood (5Ys) (3-12ms)	• at birth → Collodion baby	• at or shortly after birth (غالباً مولود بقشيرة) (< 3ms)
Course: (Age / Seasonal)	• improves ē Age & show Seasonal Variations (Winter > Summer)	Constant ē Age & shows Seasonal variation ثابته	• as Lamellar. ثابته
C/P (Scales / Site)	• Scales ch: Fine - Very rough. • Site: - Usually: → Trunk & extensors • May be at: Palm & Soles • Sparing: XX ! Face (d/t Seb. secretion) & Flexures (d/t Moisture)	• Scales ch: large, dark brown, plate like → chic Mosiac or bark-like or Fish appearance. • Site: Generalized ē Accentuatⁿ at ↑↑ flexures. Collodion baby at birth —2-3w→ the membrane desquamate → Lamellar Icthyosis (ē chic scales)	• Scales → large, dark, Polygonal chic → dirty appearance "شكلها اللى مش بيستحى" • Sites • Usually at:- [• Trunk • extensors] [• Neck (dirty Neck dis) • Ankle] • May be: at Flexures • Sparing: Face X (except preauricular area it is Pathognomonic) & Palmoplantar X
Ass.	Fillagrin • AD (وهم بره) • KP (Keratosis pilaris). • PPK • Refsum's synd.	[• Ectropion (مرزة بره) • scarring Alopecia] [• PPK • Naie dystrophy] • Rud's & Sjogren Larsson synd.	[• Corneal Opacity (10-50%) (ASYmpt) • Testicular abnormalities:] 20% ← • Cryptorchidism ♂ only • Hypogonadism • Cancer Testis • Kallman synd. • Multiple sulfatase deficiency

Antibiotics (على طول) X — ↑ staph Colonizatⁿ at flexure → Inf & bad odour

NB. Bathing suit Icthyosis: Type of lamellar affect the Warmer areas.

. Non Bullous Cong. I.E (NBCIE) (IE)

. AR, Collodion baby at birth —2-3 ws→ fine scaling & Erythema —مع الوقت→ ↓↓ Erythema ē scales persist.

. Very similar to Lamellar Ichthyosis but differs in:

1- Erythema
2- fine scales
3- Less Ectropion
4- No scarring Alopecia
5- HP: Hyperkeratosis + Normo or Hypergranulosis
6- +ve PAS & Lectin staining of st. Corneum
7- More common & ± improve ē age.

(ass) — 3, 4

Ass:-
- PPK
- Alopecia
- Nail dyst.

• BCIE = Epidermolytic Hyperkeratosis (AD):

الاسم اكبر

مسمي الاسم له (3) مكوناته

1- Bullae (& Erosion)
2- Erythema
3- Scaling..

• Bullae & Erythema ↓↓ ē Age while Scaling ↑↑:-

. ↑ Hyperkeratosis: →
. yellow-brown waxy (Corrugated) scales at Flexures, abd. & scalp; Sometimes forming spines (hystrix)
. Verrucous plaques (at) bony prominences When dislodged → (Erosion) → reform all again.

لازم اعمله — PPK (60%) → "in K1 Type"

"Antibiotics لازم اعمل" — ↑staph Colonizatn at flexure → Inf & bad odour.

NB. Bathing suit Icthyosis: Type of lamellar affect the Warmer areas.

Types

2. Defect & Pathogenesis in Each Type. (Etiopathog)

1- Vulgaris $\xrightarrow{defect}$ Filaggrin.

2- Lamellar $\xrightarrow{"}$ TG1 Enz. $\}$ → Defect CCE (Epid. barrier)

3- X-linked $\xrightarrow{"}$ Steriod sulfatase Enz.

4- BCIE $\xrightarrow{defect}$ K1 & 10.

5- NBCIE $\xrightarrow{"}$ Unknown. Ct ← TG-1 ↓ ↑ Expression of K6,16,17) ; Hyperprolif Ks ↓

Cell Kinetics

- in Types 1,2,3: NL cell kinetics
- "Retention Hyperkeratosis"
- Types 4&5: ↑↑ cell kinetics "Hyperproliferative Hyperkeratosis"

NB:-

(1-) IV (another defect): ↓ serine protease → persistence of DSG1 → Retent⁻

(2-) XLR: Defective steriod sulfatase →:-

(a-) Failed dissolut⁻ of cholesteral sulfate (Mortier) → Retent⁻

(b-) Failed deConjugat⁻ of DHEA-S of placenta → ↓Estrogen → Failed Cx. dilatation → تبول بصعوبة

3. Pathology

1- Vulgaris:-

- Hyperkeratosis (ē follicular plugging)
- → ⊙ Hypogranulosis (ē↓ KH granules → ↓ Filaggrin)

2- Lamellar: (not diagnostic):-

- Hyperkeratosis
- Normogranulosis.
- ±Ve PAS & Lectin of st. Corneum (NBCEI → Both +Ve).

3- XLR:

- Hyperkeratosis
- Normo or Hypergranulosis.

4- BCIE = Epidermolytic Hyperkeratosis or granular degenerat⁻

- granular layer shows: Perinuclear vacuoles, large clumped KH grs., Cytolysis (or) Rupture → inter & intracellular spaces ē Blister format⁻ [suprabasal]

perinuclear to the vacuole, → indistinct cell boundaries & lightly staining material on K.H. clumping.

5- NBCIE:

- Hyperkeratosis Normo or Hypergranul PS. epid. Hyperplasia Paracerat⁻

Collodion baby & Harelquine fetus

C/P New born infant ch BY :-

1- Covered by membrane : (Contricting) Collodion or Parchment like. (ورقة سلوفان)
→ 1-2 Ws → Fissured & Peals → Icthyosis (بعد كدا تقع)

2. Skin : baked apple.

AET
1- CIE (non bullous) → Commonest
2. Lamellar Icthyosis
3- Nethertons synd
4- Conrad's synd
5. Idiopathic or Isolated

Complications
- Infection.
- Hypothermia.
- Electrolyte im balance.

(d.t cut. fissures & impaired function)

Tt
1- High Humid enviroment (Help separation of sloughs).
2. Daivonex
3- Acitretin (مهم)

Harlequine fetus.

def Severe form of Collodion baby, in which the appearance of the baby resembles the «Harelquine Costume» (مثل البليا تشبه).

1- Hyper Keratotic plaques
- Generalized
- Hard
- Massive
- Fissured

(armor-like)

2. **2 E**
- Ectropion.
- Eclabium (lips).

3- **2 R**
- Rudimentary ear.
- Rarely survive > 1 Ws

Tt غالباً بيموت ف أول أسبوع

Collodion baby (sausage skin)

Def: AR condition in which the baby is born covered with /or encased in a constricting, taut, shiny and transparent membrane formed by the thickened st. corneum that resembles a plastic wrap (sausage skin) then 2-3 w collodion membrane undergoes desquamation or peeling → Icthyosis (usually lamellar or NBCIE). Collodion babies are usually borne premature.

"شكل السلوفان" أو "الكيس البلاستك"

Causes:

- The two most common diseases are: (AR)
  - Lamellar ichthyosis (Few)
  - NBCIE (80%)
  - Self Healing (20%)

Other rare conditions include: NL / Netherton / ED / PIBIDS
  - Sjögren Larsen syndrome
  - Gaucher Disease type 2
  - Hay-Well syndrome
  - Trichothyodystrophy
  - Comel-Netherton syndrome
  - Ectodermal dysplasia
  - Neutral lipid storage disease. (NLSD)

NB: However 10% of collodion babies have normal underlying skin – a mild presentation known as '*self-healing*' collodian baby.

Pathogenesis: Bolognia P.754 · HP: as (IV)

Complications → physical Constraints / Drying up → Cracks → # Barrier

A- The taut membrane acts like a thick film causing physical constraints of underlying tissues →: affect / :

- Suckling and nutrition
- Breathing
- Ectropion.
- Constriction bands resulting in reduced blood supply and swelling of the limbs.

B-As the collodion membrane dries up it can crack leading to fissures → affection of the barrier function of the skin →:

- Infection
- Overheating or cooling
- Dehydration

Management

1- Admission to The neonatal intensive care unit (NICU).

2-An incubator provides: a humidified/neutral temperature environment.

3. IV Fluid & Tube Feeding.

"skin softening" → 4-keep the skin soft and reduce scaling ;The collodion membrane should not be debrided (pulled off). Treatment may include:

- Emollients .
- Pain relief such as paracetamol.
- Mild topical steroids to reduce secondary inflammation.
- Artificial tears if there is severe ectropion.

The life expectancy and difficulties that the collodion baby faces depend upon the particular underlying condition.

على حسب كيس ايه بتعاني منه

Harlequin Icthyosis

AR

(Harlequin baby) اكيليا تشو

Def. Very rare severe form of congenital icthyosis or collodion baby in which the appearance of the baby resembles "Harlequin" (clown-like appt)

Pathogenesis: uknown (Defective: ABCA12 gene → defective release of lipids from Lamellar grs → Hyperkomification)

C/P: 1- Hyperkeratotic plaques: massive, generalized, hard and fissured. → "Coat of armour"

(2E) 2- Ectropion and Eclabium. → Lip Eversion

(2R) 3- Rudimentary ear.

4- Rarely survive >1 W.

ttt→Acitretin.

معظم المرضى

• BCIE = Epidermolytic Hyperk. [بثور ← Bullae Erythema scaling]

[له نوعين من Ichthosis لها علاقة به]

• Ichthosis bullosa of Siemens

(1). Neonatal onset (Not at birth)
(2). (No) Erythroderma Nor PPK.
(3). تكون بثور وتقشر الجلد : Bullae (& Molting & fragility)
+
(4) K2 Hyperkeratosis.

Hystrix=Spine

• Ichthosis Hystrix of Curth Macklin (K1)

(Not) at birth
(No) bullae, (No) Erythrod.
→ only Hyperkeratosis +PPK
(BCIE) زي المرحلة المتأخرة من
→ Vacuolated binucleated KCs at dermis

Acquired ichthyoses
(Acq. or late onset icthyosis vulgaris)

سؤال امتحان

Def. Acquired or late-onset ichthyosis is a rare and significant occurrence, as it is generally associated with underlying pathology such as malignancy.

Epidemiology: *Age: usually adulthood however, age-associated systemic diseases do occur in children.

*Sex and Race: no predilection.

C/P: as Congenital Icthyosis vulgaris.

Causes:

A-Malignancy: (Acq. *Icthyosis is a paraneoplastic syndrome*):

—Leukemia

—Lymphoma:

* Hodgkin's (The most commonly reported malignancy, the skin lesions as a rule occur simultaneously or after the lymphoma is diagnosed)

*Non Hodgkin's (lincluding MF).

—Sarcomas (Kaposi sarcoma, lymphosarcoma, leiomyosarcoma)

—Carcinomas (breast, lung, colon, etc.,....)

—Multiple myeloma. (MM)

B-Drugs:

-Retinoids (*Antiandrogen effect→↓sebum*).

-Cimetidine (//)

→Clofazimine (Leprosy)

-Niacine (*and antihypercholesterlomics*)

-INH.

-Allopurinol.

C-Nutritional:

-Pellagra.

-Kwashiorkor.

-Hypo and hypervitaminosis A.

-Deficiency of Linoleic (important constituent of epidermal lipids)

D-Metabolic:

-CRF (→*Hypervitaminosis A*)

-Hypothyroidism.

-Panhypopituitarism.

E-Miscellaneous:

-Leprosy(LL)

-Syphilis

-SLE

-Dermatomyositis

-HIV

-Sarcoidosis

-Polycythemia

- Leprosy → itself Clofazimin as Tt
- Malignancy

Treatment of Ichthoses:-

1- Tt of Cause [in Acquired Type]

2- Emollients & Keratolytics

3- Acitretin & ± Isotretinoin

4- Liarazole: (S.E & Teratogenicity are as Isotret.)

دكتوراه جديد

Liarazole:-

- Retinoic acid Metabolism Blocker
- ..cyp26 dependent Hydroxylation of all Trans. Ret. acid → ↑ level
- → 75-150 mg ¶ d

Syndromes with Ichthyosis
(Icthyosiform synd)

كلام كتابي للدكتورة (3,4,5,6 الـ سنتر 7)

- 1- Refsum's
- 2- Rud's
- 3- CHILD
- 4- KID
- 5. HID
- 6- BID
- 6- Netherton (مرجع مهم)
- 7. Sjogren-larsson
- 8- Conradi-Hunerman
- 9- Chanarin-Dorfman
- 10- Multiple sulfatase deficiency.

[3, 4, 5, 6, 7] لو عاوز تحفظ بسهولة يبقى أول أنواع:

(1) 1- Refsum's (AD) [الحروف الأولى]

- I. Vulgaris
- Anosmia, Ataxia, Deafness, Retinitis Pigmentosa & CVS (حواس)
- Nerve → Deafness
- WBCs → Vacuolated (للتشخيص بالدم) Fibroblasts
- Cataract
- Skin (LI or NBCIE) + Lipid droplet on Biopsy.

(2) Rud's synd. (AR)

- Lamellar Ichth.
- Retinitis pigm. (عين)
- CNS → Epilepsy & MR
- Infantalism.

5, 6, 7

CHILD

- XLD
- Cong. Hemidysplasia
- Ichthyosis
- Limb defect

[NBCEI بس شكلها الكتابية ILVEN]

KID

- Keratitis
- Ichthyosis
- Deafness

(AD)

HID

- Hystrix Like Ichth
- Deafness

(3) Conradi Hunerman.

C
C
Blaschk.I
XLD

- XLD "مرة" (W3BHSD) (XLD عظام عين)
- Cataract
- Chondrodysplasia punctata: (عين عظام)
- premature calcification (Trachea & Verteb.) → stippling ē XR
- Blaschkoid Ichthyosis → Follicular Atrophoderma.

photosensitivity / Ichthyosis → PIBID (Brittle Hair, Intellectual impairment & decreased Fertility)

- AR, ERCC2/XPD gene defect →:
  1. defective DNA repair → photosensitivity
  2. defective sulfur content →
     - ✓ Tiger tail (الشعر فاتح وغامق = مخطط)
     - Trichoschesis
     - Pili torti

(4) Chanarin Dorfman (AR)

- NLSD = Neutral Lipid storage disease ch by Accumulation of (TGs) in Many organs:-
  - Liver → HSM
  - Muscle → Myopathy

TGs تتراكم

(9) Sjogren Larsson (AR)

(White) تذكر كلمة

White (أبيض) —
- Matter dis. of brain → plegia
- perifoveal white glistering dots → في العين

10- Multiple Sulfatase Deficiency

(Austin dis) · [AR]

· Due to SUMF1 Gene Mutat^n → defective sulfatases enz. group (including steriod sulfatase).

→ Accumulat^n of:-
- Glycosaminoglycans (GAG)
- Glycolipids (GL)
- Glycopeptides (GP)

→ ↑ urinary:-
1- oligosacchrides
2- MuCopolysacch.
3- Sulfatides.

CIP
1- Ichthyosis (lamellar).
2- Course facial features.
3- Deafness.
4- Hydrocephalus.
5- limited Elbow extension.
6- Neurological complicat^n.

Q. NB: (شفوي مع دكتوراة)

① Ichthyosis + Deafness:-
- Refsum's, KID, HID, CHILD ⁉
- Chanarin-Dorfman (NLSD)
- Sjogren-Larsson. (SLS)

→ XLRI

② Ichth + Eye: LI, Refsum's, NLSD, SLS, Tay's synd, KID

③ " + Neuro: NLSD, SLS, Refsum, " , IFAP

④ " + Hair: Tay, Netherton, KID, IFAP.
- Ichthyosis follicularis
- Atrichia
- photophobia

+ PIBID

Netherton Syndrome

(Trichorrhexis invaginata, Icthyosis linearis circumflexa)

Def. Rare (AR) genodermatosis characterized by:

1- Congenital ichthyosiform erythroderma (NBCIE)
2- Trichorrhexis invaginata (Bamboo Hair) [= Ball & socket]
3- Atopic diathesis (AD)
4- Failure to thrive. (FTT)

Ichthyosis → NBCIE + Ich. linearis circumflexa.

Etiology and Pthophysiology:

للماستر → mutations in the SPINK5 gene that is found on chromosome 5. → disturbed ↓ Epid Hair shaft ↑ Matura & Keratiniz

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CIP

(1) Ichthyosis: at first: NBCEI (but (No) Collodion baby)
then: "Ichthyosis Linearis Circumflexa"

→ Migratory, Serpigenous, Annular or Polycyclic double edged scaly lesions at Trunk & proximal limbs.

(2) Trichorrhexis Invaginata:-

- Bamboo hair or Ball & Socket — distal shaft = ball; proximal " = socket
- also: ± pili torti

(3) Atopy (بأي نوع..)

(4) Failure to thrive: d.t Associated Enteropathy.

(5) others: ↑↑ IgE, ↑↑ Eosinophils, ↑↑ susceptability to infect°, dehydrat° & Electrolyte Imbalance ↑↑

- Diagnosis:
  1- Hp
  2- Genetic diagnosis
  3- LM & EM of Hair
  4- Lab: ↑ IgE & Eosinophils

⊙ TTT:- 1- Hair (علاج)
2- Systemic manifs. (حسب الأعراض)
3- Ichthyosis:- نفس العلاج السابق

MSUI

Erythrokeratoderma

(Erythrokeratodermia)

- DNNZ
- Sicurezy

AD but ± sporadic

Def. Group of Genetic disorders caused by Mutations in (Connexin Genes) (Gap Junct^ protein beta3) → (disordered Keratinizat^) that ch- clinically by Erythematous Scaly Plaques.

Types → KIDs

Mendes da Costa's synd.

Erythrokeratoderma variabilis (EKV)

- at birth or Neonatal period & (may) improve at puberty or stabilize

غالبا مستمر لكل حياة

- of 2 Types of plaques

- **Fixed Hyperkeratotic**
  - Maope like or figurate at extensor arms & Legs.

- **Migratory Erythematous**
  - at any sites
  - lasts for hours - ds or wks then either Fade or Migrate to other areas.

- May be asympt. or ass e < itching & burning
- Both ass (e) ppK.
- ppt Factors:-
  - Stress
  - Frict^
  - Temp changes

Gottron's synd.

Progressive Symmetrical Erythroketatoderma

- onset: infancy or Early childhood.
- Resolut^: (as in EKDV)
  Fixed for life Extend to stabilize after puberty.
  يعني تضل المرض بدون ظهور حالات جديدة بعد البلوغ

- as EKDV but:
  1- No Migratory plaques
  2- More at Shoulder Girdle & buttocks
  3- Hands & Feet often involved (Uncommon in EKDV).

✓ ACitretin is the ^th of Choice

سؤال امتحان

Epidermolytic hyperkeratosis

Definition: There is an increase in the thickness of the granular layer, where keratinocytes contain increased number of keratohyaline granules. Perinuclear vacuolization occurs in this area, and the cell boundaries may be indistinct. If vacuolization becomes marked it leads to intraepidermal vesicle formation. The stratum corneum shows hyperkeratosis.

- No large clumped

BCEI

→ The condition occurs in: bullous icthyosiform erythroderma, Mal de Meleda keratoderma, epidermolytic acanthoma, ILVEN, verruca vulgaris, naevus comedonicus, solar keratosis, seborrhoeic keratosis, and incidentally with tumours as basal cell papilloma and SCC.

- BCEI, Sjemeay KID
  - Keratoderma (Maldem)
- ILVEN
  - Nevus Cond..
- AK
- SK
- Warts
- Tms
  - SCC
  - Bcp

(GG1) # Palmoplanter Keratodermas (ppks)

(Tylosis) (keratosis palmaris et plantaris)

Def. group of Hereditary & Acquired disorders in ✓ there is Hyperkeratosis of palms & Soles.

introduct°. Basics of Keratin & connexins (HL → (P 770)

Classification of ppks

(مثال امتحان)

1- Hereditary ← diffuse, focal, punctate.
2- Acquired
3- Erythrokeratoderma
4- Ichthyoses + keratoderma.
5- Ectodermal dysplasia + "
6- others.

(HL) ←

Some definitions:-

- diffuse ppk → uniform pp thickening
- localized " (Focal) → localized thickening located mainly on pressure areas & acc. to shape of lesion
  1. Areata / Nummular → oval ppk.
  2. striata → linear ppk (mainly on palms)
- Punctate " → small (1mm-1cm) keratotic papules.
- Transgradient: pp affect° ē extension of keratoderma on To the dorsum of Hands & feet.
- Non Transgradient: only Palm & Soles ē (no) upward Extension.

Hereditary PPKs

Diffuse

Isolated

(1) Epidermolytic PPK (EPPK)
(Vörner)

Non Epidermolytic (NEPPK)
(Unna-Thost)

- Mal de Meleda
- Greither
- others:-
  - Nagashimi
  - Gamborg-Nielson
  - Sybert.

Ass ē other features

- Vohwinkel synd
  - Olmsted "
  - Papillon Lefèvre "
  - Hydrotic Ectodermal dysplasia
- Naxos synd
- Huriez synd.
- Bart Pumphrey Synd.
- PPK ē Sensorineural deafness.

Focal

Isolated

Numular or streaky oval (Nummular) or linear

(1) Focal/Nummular or Areata PPK

(2) striata PPK.

Associated other Features (Synds)

- Howel-Evans
- Pachyonychia Congenita (PC)
  - Richner-Hanhart
  - Carvajal
- Focal PP & Gingival Keratosis.

Punctate

- Isolated
- Ass ē other features

PPK مفصل

See the classificat-

A- Hereditary

1- Diffuse Isolated PPK

All AD except:- Mal de Meleda

Vorner (K1, K9) / Unna Thost (K1):

- Commonest 2 Types
- Non Transgradient
- Path → the same but:
  - Vorner: Epidermolytic Hyperkeratosis
  - Unna: Non Epidermolytic Hyperk.

Mal de Meleda (Keratosis Palmari et pla)

- Both Transgradient at PP, Elbow, Knee — epidermolytic Hyperk in Path
- Meleda: 2 chic:-
  - (2P) PP Hyperhidrosis → Bad odour
  - Periorifacial lesions (less severe than olmsted)
  - MR

Greither → (تحت الصمت؟)

- PPK
- Hyperhidrosis
- Achilles & elbow & Knee

- Transgrad. & progradient (progressive)
- chicolly → affect Tendon Achilles
- ass. → Elbows & Knees Hyperk
  - → Hyperhidrosis

- Mal de Meleda, Greithers → Transgradi PPK, Hyperhidro
  - Mal: Perifacial
  - Greith: Tendon Achills, Elbow & Knee

- All are AD except: (AR)
  - Mal de Meleda
  - papillion Le-favre
  - Naxos
  - Carvagal
  - Richner-Hanhart
- olmsted → unknown

(2-) Diffuse PPK ē ASS:

Features (AD اللي فوق و اللي تحت)

Vohwinkel PPK (Mutilating PPK) [AD] — حرف (H)

- Honey-colored PPK ē star-fish Keratoses at dorsal Hand.
- Pseudoainhum الصوابع
- Hyperkeratosis (Linear at elbow & knee)
- Hearing loss.

Olmsted (AEP ...) (??) — حرف O

Olmsted → Orifacial

· Mutilating PPK ē Periorifacial Keratotic Plaques + Cancer (SCC, MM)

Papillon Lefèvre (AR) — Periodontitis, Psoriasiform, Hair, Nail — تذكر حرف P

- Periodontitis (ē teeth loss)
- Psoriasiform Lesions
- Nail & Hair.

Naxos (قلب و شعر)

· Woolly Hair & RV (Right Vent) Cardiomyopathy.

Huriez (قلب صوابع) — حرف (S)

· Sclerodactyly ē superimposed SCC

Hidrotic Ectodermal dysplasia (Clouston) (AD)

PPK – Nail dystrophy – Hypotrichosis (ثلاثية)

infancy ē شعر يتقع
و بعدين يبقى طبيعي
و تسقط شعر عند الطفولة
أو البلوغ

Bart Pumphrey Synd.

- PPK
- Knuckle Pads.
- Leukonychia
- Deafness.

3- Focal (localized) PPK

Isolated
معزولة

- Atrata
  - Vapor Nummular Hyperk.
- Striata
  - Linear
  - Islands of Hyperkeratosis

Associated w other features
(AD) الى فوق و الى تحت

- AD — Howel Evans → PPK w Esophageal Carcinoma (بعد سن 40)
  - NE-PPK
  - A. عالية الخطورة High risk
  - B. بدون Bg
  - في تايوان
- AR — Carvajal
  - Left Heart
  - Wolly
  - PPK (striate) + Woolly Hair + Cardiomyopathy (left sided)
- AR — Richner Hanhart (Oculocut Tyrosinemia)
  - PPK + Eye + MR
    - Focal Painful
    - dendritic Keratitis
    - Tyrosin Crystals (by slit lamp)
  - MR: تخلف عقلي Tyrosinemia
- AD — Pachyonychia Congenita (PC)
  - موجود بـ PPK
  - تذاكر تفصيلها

④ Pachyonychia Congenita: (PC)

(سمك الأظافر) (Short)

- def. AD Ectodermal dysplasia ch. By "Hypertrophic" Nail dystrophy.

- Epidomiology : Age = usually at birth but may appears Later on (PC Tarda) at 10-30 ys.

- Sex, race → (No) specific predilection

- Types of PC:-

incid. of Manifs.	
. PPK	90%
. Nail	70%
. Follicular H.	5%
. Hyperhidrosis	50%
. Leukokeratosis	30%
. Blisters	20%

① . Type I (Jadassohn-Lewandowsky Type) :-
dt Mutat^n in K6a & K16

② . Type II (Jackson-Lawler Type) :-
dt Mutat^n in K6b & K17

③ PC-III
Tarda

CIP
[1] PC-I ← skin, Nail, MM

[1]- skin : . PPK (Focal, NEPPK) ass. e → Hyperhidrosis, Blister on fricta & Moisture.
PPK-KP
. K-P (90%)

[2]- Nail: أول حاجة تظهر في خلال السنة الأولى أو الثانية (أول سنتين)
- Nail bed → subungual Hyperkeratosis shapped Thickening → Wedge
- Nail plate → Thickening, With brown discolorata
* All (Finger) Nails are affected but Toe Nails are less affected.
* (Thickening) No dystrophy (as in Dysk-Cong.)

[3]- MM : oral (Leukokeratosis) [Leukoplakia like] → Not precancerous DD Dysk. Congenita.

[4] other (lacrymix Eye) → Hoarseness & rarely resp. obst & death.
→ cataract & opacity

2. PC. II : as PC-I but differs in:-

① - Cut cysts → Steatocystoma M.
Epidermoid cyst
Eruptive Vellous Hair cyst

N ② Natal teeth.
③ No oral Leukokeratosis
④ less severe PPK & Blisters.

Treatment
1- ↓ moisture & friction
2- ttt of Hyperhidrosis
3- Retinoids

Punctate ppk

Isolated
1- Punctate Keratosis of Palms & Soles.
2- punctate Keratosis of Palmar Creases.
3- Acrokeratoelastoidosis of Costa
- <20Ys, Asympt, firm, yellow, shiny Papules at → Marginal pp / Legs, Nuckles
- Hp: Elastorrhexis

Associated
- With → Spondylosis. Lipomata. Mg

- ppk + deafness:-
✓ - Vohwinkel
✓ - loricrin ppk (Type of Voh. winkel)
✓ - Part Pumphrey
✓ - Diffuse ē Sensorineural deafness

- ppk + Hair, teeth, Nail Abnormalities:- → - Clouston, - Papillon Lefevre, - Naxos

Acquired keratodermas

Acquired keratoderma are keratodermas that are NOT inherited as a primary genetic condition. They may occur as part of a generalised skin condition (some of which may be inherited) or as a result of another illness. it more likely to present in adulthood (compared with inherited keratodermas which usually present in childhood).

1- **Inflammatory skin conditions** →
- Psoriasis PS
- Dermatitis (eczema)
- Lupus erythematosus LE
- Lichen planus LP
- Pityriasis rubra pilaris PRP
- Erythrokeratoderma EKD

2- **Infections** →
- Reiter syndrome
- Dermatophyte fungal infection (tinea)
- ✓ Syphilis ✓
- Crusted scabies
- ✓ Extensive viral warts (usually in immunosuppressed patients)

3- **Circulatory problems** →
- Lymphoedema

4- **Secondary to inherited conditions that may not usually result in keratoderma** →
- Ichthyosis I
- Ectodermal dysplasia ED
- Epidermolysis bullosa EB
- Erythrokeratoderma EKD

5- **Medications and toxins** →
- Iodine
- Lithium
- Glucan
- Halogenated weed-killers
- Arsenic
- Chemotherapeutic agents used in cancer treatment

6- **Internal illness** →
- Myxoedema
- Internal malignancy (2M)

7- **Miscellaneous** →
- Keratoderma climacterum.
- Aquagenic keratoderma.

PS
ECZ
L.P

fungal
viral (WW)
parasitic

✓
SLE
ICH
EKD

inv
4 ✓

Acq. Keratodermas

- Keratoderma climactericum
- Aquagenic Keratoderma
- Keratoderma with MYxedema
- Keratoderma with Cancer.

(اليأس) **[1] Keratoderma climactericum:** سن اليأس عند السيدات — 3 < Menopause, obesity, xerosis. There is painful fissures at pressure points

- Age > 45 Ys or Young ♀ after oophorectomy
- C/P: Hyperkeratosis starts as pressure Points → extends with Severe fissures & painful Walking
- aggrevating factors → obesity & dryness.

Tx:
1- Systemic:-
  - Estrogen Replacement therapy (ERT)
  - Retinoids

2- Topical:-
  - Estradiol 0.05% oint
  - Urea: 25-40%.

(المية) **[2] Aquagenic Keratoderma:-**

- Thickening & white Transulucent Pebbly "sep" changes → Shortly after Immersion in Water (خلال دقائق ويختفي دقائق بعدها)
- usually ass. ē → Burning sensat° & Edema & Hyper-hidrosis
- Age: 20-30 Ys.
- Path: NL skin or mildly dilated Eccrine ostia & Hyperkeratosis.
- Tx → Tx of Hyperhidrosis → rapid improvement → 20% Aluminum Chloride Hexahydrate.

ملخص
Adults.
(i). thickening ē + white Transl. pebbly
(ii). Edema
(iii). Burning
(iv). Hyperhidrosis

3- Keratoderma with Cancer:-

- ppk may be ass. with Cancer in following conditions:

(ex)

1. Howel Evans → focal NEPPK + Cancer Esophagus
2. Huriez Synd → PPK + SCC on Atrophic areas of skin
3. Mutilating Keratoder (olmsted) → Epitheliona Caniculatum
4. Tripe palms → adenocarcinoma of stomach / Lung
5. Arsenical → small Corn like areas of Hyperkeratosis on pp surface → ↑ size & No → ulcerate & Mg

يحدث بعد تناوله عن طريق الفم بفترة 10-30 سنة

6. Acquired ppk → may be ass. ē Carcinomas of Lung / Breast / Colon
7. Spiny-Keratoderma: Carcinoma of

def: deceptive term indicating "Velvety Thickened Palmar skin with exaggerated NL dermatoglyphics"

4- Keratodermas with Myxedema:-

- Hypothyroidism may be aware cause of ppk
- thyroxin ↑↑ → improvement

---

* ↑↑ of ppk:-

1. Emollients
2. Keratolytics (6% S.A in 70% Propylene Glycol)
3. Topical retinoids
4. Topical vit D (Calcipotriol)
5. Systemic retinoids.
6. Acq. ppk → ↑↑ of the cause..

Pityriasis Rubra Pilaris (PRP)

(Lichen RP, Lichen Ruber Acuminatus - Devergies dis)

Def : chr. papulosquamous disorder ch By:-

1. Diffuse scaly scalp
2. Localized follicular Hyperkeratosis
3. Psoriasiform, scaly, (reddish-orange) plaque
4. PPK
5. Nail changes.

لو كلهم موجودين مع بعض يسمى

(Typical or Classic PRP)

- Epidemiology : - Age → 2 Types of PRP

ACq (١) نوع الأطفال – Inher (٢) نوع البالغين

- Familial (AD but ± AR) ↓ الطفولة • 1 Peak: Early Childhood
- Acquired ↓ • 2 Peaks 1st & 5th decade. سنه ٥٠ او ١٠ سنه

- Sex & race → (No) predilectⁿ.

- Etiopathogenesis :- Unknown but ±:-

1. Familial (AD or ± AR). CARD gene Mutatⁿ
2. AbNL keratinizatⁿ & Vit A Metabolism
3. Minor Trauma.
4. UVL
5. Inf (strept) [as a Super Ag] ← عمله كيف قبل المرض.
6. Immunological
   - Autoimmunity : PRP ± ass ē M G, Myosites or Hypothyroidism.
   - AbNL response to Ag (ass ē HIV (or) Int Mg)

- **C/P:- →**

(1) Diffuse scaly scalp (SD like, common initial clinical Manifs.)

(2) localized Follicular Hyperkeratosis:-

→ Key finding of PRP.

← Rough Follicular papules on erythematous base (nutmeg grater like)

on dorsal aspects of fingers (but ± at < extremities / trunk)

(3) psoriasiform plaques:- < Red-red orange Islands ± Erythroderma

- red - red-orange scaly patches & plaques on Trunk & extremities ē areas of sparing "Islands of sparing"

- may progress to Erythroderma.

(4) PPK (red-orange, Waxy Keratoderma) at foot: [PRP Sandal]

(5) Nail changes: < thickening. discolorat^ : Yellow brown.. Subungual Hyperk.

(6) others: MM (Lp like), Hair (Alopecia) & Ectropion

- **Types (classificat^) of PRP** (Griffiths classificat^ based on < Age / durat^n / Type of Cut. involvement.)

(1) Type I (Classical adult)

- Most Common Type (>50%)
- Self limiting (80% in 3 Ys)

(2) Type II (atypical adult): as Type I but differ in

- less Common (5%)
- less self limiting (20% ein 3 Ys)

- less < Alopecia, Ichthy & Alopecia

- Additional manifs:-
  - PPK ē Coarse (lamellated) scales.
  - Icthyosis of L.L
  - Alopecia.

3. Type III (Classic Juvenile):-
   - 10% of Cases.
   - Very similar to Type I.

4. Type IV (Circumscribed Juvenile):- مميزاتها < Most common / No Eryth.
   - Most Common Juvenile type: ✓
   - localized (never generalized as the other Types)

5. Type V (Atypical Juvenile):-
   - Similar to type II (but ē) More → Icthyosiform scales, (chronicity), Sclerodermoid of Fingers.

(Recently) → 6- Type VI [HIV ass Type]
   - Ass. ē HIV
   - [± ass. ē:] Acne Conglobata, HSV & Elongated Follicular Spines.
   - resistant to Conventional therapy of (PRP) but ±
   - (±) respond to HARRT.

- Pathology: (Not Specific) (useful to exclude other papulosqu dis)

(مختلف عن PS)

① Hyperkeratosis alternating (ē) orthokeratosis & parakeratosis [checkerboard like] → رقعة الشطرنج

② Hypergranulosis

③ follicular plugging ē perifollicular Parakeratosis → shoulder effect. (أهمهم ١٢٣ / ٥)

④ broad rete & Narrow dermal papillae.

⑤ Acantholysis (adnexal) ē focal Acantholytic dysk

EIM → ↓ KIF & Desmosomes.
→ Parakeratosis ē lipid like Vacuoles.
→ ↑ K-H grs
→ Split at Lamina basal

D.D:- ① Psoriasis :-

- red-orange ppk, follicular Hyperk, Islands of sparing → absent in Ps. Vx

- Hyperkeratosis
- Follicular plugging
- Acantholysis
- No Neut.

→ Ps. Path (Acantholysis ē focal acantholytic dysk. → PRP)

② SD (other PRP features are absent) resistance to usuall Hx of SD → PRP)

③ PRP like erupt⁻ may be:
seen in DM pt. (Wong Type).

④ Kawasaki

⑤ symmetric progressive Erythrokeratoderma

⑥ other causes of Erythroderma..

Hx → Empirical
- Best: Retinoids
- 2nd MTX (Retinoid Resistant Cases)
- Phototh: Combined ē Retinoids

① Vit A : → كان بيتاخد أيام زمان
Vit A ولكن كان جرعات كبيرة سمية
Toxicity ← اتلغى هذا العلاج

② Retinoids (الأفضل)
Topical & systemic
- Isotr 1-1.5 mg/kg/d for 3-6 ms)
- Acitretin.

③ MTX (10-25 mg/w) if Resistant to Retinoids

④ MTX + Retinoids → in severe cases

⑤ other lines
- Emollients, Cs
- Topical Vit D
- Immunosuppressives: Cs (Topical & Syst)
  - Azathyo
  - Infliximab
- Anabolic steriods [in response to ↓↓ Serum level of PRP]
- phototherapy → may exacerbate PRP so better avoided or Combined ē Retinoids given

UCP

Perforating Dermatoses

Def. Group of papulonodular skin disorders ch' By Keratotic plugs or Crusts in dermal CT: " perforates" or is eleminated through epid.

- Collagen
- Elastic or Necrotic organism, ..

(1- 1ry or) MAJOR PERFORATING DISEASES

Disease	Incidence	Time of onset	Location	Perforating substance	Associations
Reactive perforating collagenosis (RPC), inherited	Very rare .Transient	Childhood (AR)	Arms, hands, sites of trauma	Collagen	None
Elastosis perforans serpiginosa (EPS)	Rare, M>F .persistent	Childhood, young adulthood; variable with penicillamine-induced	Neck, face, arms, areas other flexural	Elastic tissue	Genetic diseases (see Fig. 95.13), penicillamine
Perforating folliculitis	Common	Young adulthood	Trunk, extremities	Necrotic material	May simply be ordinary folliculitis with follicular rupture, i.e. not a specific entity
Acquired perforating dermatosis, includes acquired RPC, Kyrle's disease[*] and, occasionally, acquired EPS	Common (10% of dialysis patients)	Adulthood	Legs or generalized	Necrotic material, collagen or, uncommonly, elastic tissue	Diabetes, renal disease, pruritus, rarely liver disease; may be end stage of perforating folliculitis
Perforating periumbilical calcific elastosis (Perforating Calcific elast)	Very rare, (more common in black women)	Adulthood	Abdomen, periumbilical	Calcified elastic tissue	Multiparity

(2) 2ry / Incidental: GA, NBLD, Sarcoidosis, Calcinosis, MF, Melanoma, Paget's, Gout, FB react.

- Etiopathogenesis: of Transepidermal Elimination

⊙ the epid. becomes hyperplastic & surrounds the abNL CT, just as it appears to do with Wood splinters & other FBs.

- ⊙ in Acquired perforating dermatosis: pruritus & chr itching → epith. hyperplasia (as in Prurigo Nodularis, so many patients have both diseases)

Familial ↓ Discussion

1- Reactive perforating Collagenosis (RPC):-

- rare familial disorder (AR)
- start in childhood.

Koebner → . Superficial Trauma $\xrightarrow{3-4\text{ws}}$ 5-8mm, Keratotic Papules

usually on < Hands / arms $\xrightarrow{6-8\text{ws}}$ spontaneous resolution

- Varieties:-

Non-familial Severe Trauma Verrucous Papules

(1) Linear Type (Koebner).

(2) Verrucous Types

(3) Acquired Type: in adulthood, ass ē DM or RF (so better classified as Acq. perf. dermatosis but its Histopath is identical to familial RPC)

NB
- Eliminated material is Collagen
- Koebner: is seen in all types of perforating dermatoses (but) More Marked ē RPC.

2- Elastosis perforans Serpiginosa (EPS):-

- Childhood or Early adulthood.

→ 2-5 mm Keratotic papules arranged in Serpiginous pattern usually on lat. Neck (& Antecub. fossa but + Face, Neck, arms, Flexures)

→ usually persist for several years (some cases may show spont. resolution)

- it may be ass with: Genetic, drug, RF

1- Genetic diseases (4%)

- Down synd
- Marfan "
- Ehler-Danlos
- osteogenesis Imperfecta
- PXE
- Rothmond Thomson synd.

2- D-Penicillamine associated.

3- RF or DM (Acquired Perf dermatosis)

③ Acquired perforating dermatosis:

- يسمى (٣) / Kyrie's dis / Acq RPC / EPS / Perf. Folliculitis (rare)] — by some authors
- It includes any perforating dermatosis ch' BY:
  1. start in adulthood.
  2. usually ass ē → DM, CRF pruritus (& dialysis) (10٪)
     rarely ass ē (الورق) → Hepatic pruritus, Malignancy, CHF
- CIP: Follicular & Non-Follicular Hyperkeratotic Papules & Nodules usually on Legs but ± Generalized.

(HL)

- Kyrle disease was first described in 1916 by Kyrle as 'hyperkeratosis follicularis et perifollicularis in cutem penetrans' or 'follicularis et parafollicularis' to emphasize that not all lesions were proved to be centered on follicles; It identified as a perforating disease. To this day controversy remains about the classification of Kyrle disease – is it a distinct disease entity, part of the spectrum of acquired perforating dermatosis or a subtype of acquired perforating collagenosis?
- Largely on the basis of their histologic findings, patients with acquired perforating dermatosis have been variably designated in the literature as having RPC[17], EPS[2], perforating folliculitis[13] or perforating pseudoxanthoma elasticum[18]. Since the pathologic findings vary from lesion to lesion in the same patient, it seems unwise to subclassify patients in this way. Since some, but not necessarily all, of these lesions appear to be follicular, and since manipulation of the lesions by patients frequently alters the histologic changes, the term 'acquired perforating dermatosis' was proposed to encompass all of these cases

④ Perforating Periumbilical Calcific Elastosis:

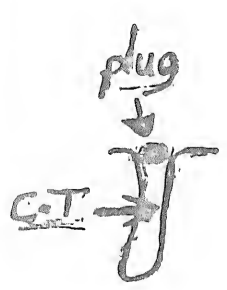
- Umbilicus → Black Multi ♀
- Breast → CRF
- Periumbilical keratotic papules usually affect Multiparous black Women. (other site: Breast) → CRF

(البولينا. بسيرس)

⑤ Perforating Folliculitis:-

- Clinically as ordinary folliculitis but ē follicular rupture
- Common ; in Adults ; at Trunk & extremities.
- Eliminated (Material Necrotic.)

Histopathology



in All Types there are → Plug of Crusting or Hyperkeratosis & Variable parakeratosis.

- inside the plug (or in epid) < Collagen fibs are seen (in Rpc)
  Elastic " " " (in Eps) → Not Calcific DD PXE
- Dermal CT around the plug shows:-
  - in Rpc → appears unremarkable
  - in Eps → ↑ amount of (brightly) Eosinophilic elastic Tissue.

Verhoeff-van Gieson stain:
- Coll → red
- Elastic → black

- Inflamm. infilt (Neut, Eos, Macrophages & Lymphocytes)

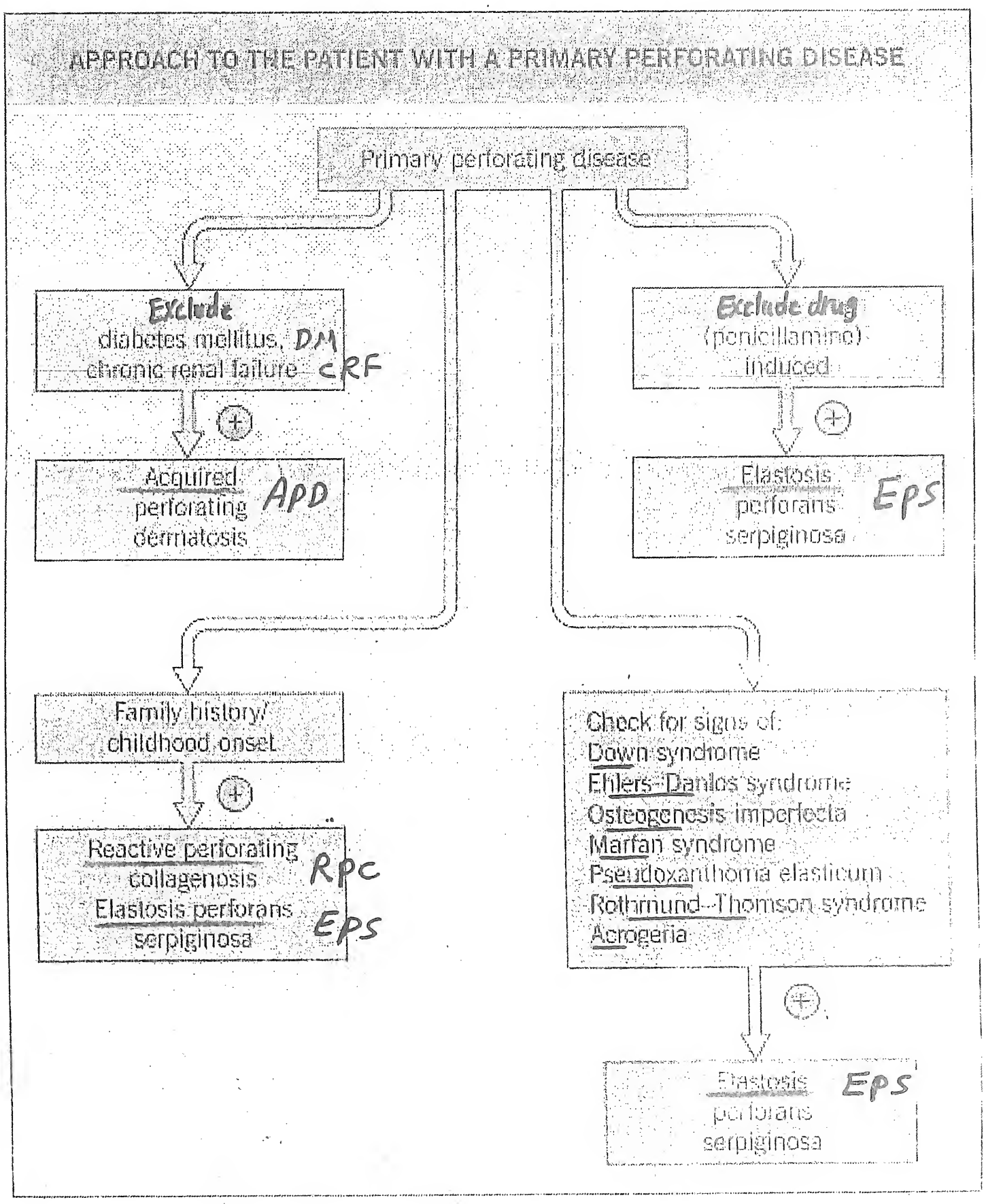
Treatment

1- Topical
- Cs
- Emollient
- Retinoids
- Keratolytics
- Benzyl peroxide
- Menthol

2. systemic
- Antihistamines.
- Cs
- Retinoids
- Antibiotics
- MTX
- Charcoal
- Allopurinol (if ↑UA)

3. Others
- Avoid Trauma
- phototherapy
- physical methods

DIFFERENTIAL DIAGNOSIS OF PERFORATING DISEASES	
Reactive perforating collagenosis and acquired perforating dermatosis	
Excoriations from a variety of causes (prurigo simplex)	
Prurigo nodularis	
Folliculitis	
Arthropod bites	
Perforating of exogenous foreign material	
Perforating of endogenous substances	
Multiple keratoacanthomas	
Dermatofibromas	
If Koebner phenomenon, psoriasis, lichen planus, verrucae	
Elastosis perforans serpiginosa (resembles other annular diseases; see Ch. 20)	
Granuloma annulare	]Common annular diseases = O
Tinea	
Sarcoidosis	
Actinic granuloma (annular elastolytic giant cell granuloma)	
Perforating pseudoxanthoma elasticum	
Porokeratosis	
Discoid lupus erythematosus	



Acanthosis Nigricans (updated 2010)

(AN)

- Def: Cut. disorder ch` By darkening & papillomatous Hyperkeratosis giving → a velvety texture usually affecting Neck & Flexures.

NB: AN is not a dis (per se) but a Cut. sign of underlying Condition or a disease.

- Etiopathogenesis: Unknown but ± d.t

① Factors that ++ Epid kCs & dermal fibroblasts:

GFR = growth factor
Epid Fibroblast.

- Insulin
- Insulin like GF (IGF)
- EGFR
- FGFR

[Tyrosine kinase Rs] → (Bg AN)

- Transforming GF-B (Secreted by ↑ Tm or in response to Tm) → Mg AN

② Perspirat~ & Frict~ → عملية كده بيحرج تفايات الجلد

③ Drugs: d.t ++ of < IGFRs / FGFRs

- Epidemiology: any but usually adults.
  - Age:
    - Elderly AN → ± Mg.
    - in children → ± Mg (Wilms Tm, osteogenic sarcoma)
  - Sex: M=F
  - Race: More in darker individuals.

- Clp. Asympt., Hyperpigmented, (velvety) thickening of skin of Neck & Flexures (Warty) excrescences ± develop.
- other sites:
  - ↓ MM (mouth, Esoph)
  - ↓ Eye (lid & conj.)
  - ↓ Areata

- often as ē skin Tap

Types of AN

(1.) Familial (Hereditary): –

- AD, d.t ↑ Insulin
- Start at childhood → Progress till puberty → Stabilizes (or) regress.

(2) Obesity associated [Most Common]

- Marker of < Hyperinsulinemia & Metabolic Synd → Insulin Resistance

تحليل — Serum fasting Insulin & HoMA Test.

(3-) Mg. ass ch by:

- Severe & Extensive.

Mucosa (25-5%)
- Mucosal & Mucocut affect^: Mucosal lesions are (not) pigmented & affects Tongue, oral Commissures, Lips & Eye.

Palms
- Palm affect^: Tripe (أمعاء) palms [Exaggerated dermatoglyphics ē Velvety (rugose) thickening of Palms]

(Villi of stomach)

> NB: Tripe palms ē Mg may occurs alone (25%)

- (Mg) → Most Common is Gasteric adenocarcinoma.
- AN usually Preceede the Mg. (60%) كلهم يكونوا مع بعض قبلها بـ ٥ سنوات

(4) Syndromic AN:

(لفع نفين السكر — Insulin resistance)

- HAIRAN Synd نفرين ((استغا))
- Autoimmune AN: Anti-IR abs.
- AICTDs

(5) Drug induced: Nicotinic acid [أوميجا], Fucidin & Cps & Cs.

(6) Unilat (Nevoid): AD, unilat, Linear (may represent unilat Epid Nevus).

للقراءة

Clinical Tips

(1)

Pityriasis rotunda

A rare disease with histology of icthyosis vulgaris and consisting of persistent single or multiple patches of circular, sharply defined icthyotic scaling, usually 2-3cm in diameter on the trunk or limbs. They develop during adulthood and remain unchanged throughout life. Emollients and keratolytics may help.

(2)

Peeling skin syndromes — Keratolysis EXF. / Keratolytic Winter Ery. — في الصيف بتجيب بعرق — peeling, Eryth → Cold stress, fever, menses.

Periodic peeling of the superficial layers of the skin resulting from damage to the stratum corneum has different causes. Histologically, there is cleavage within the stratum corneum. There are (3) peeling skin syndromes in which peeling (*keratolysis*) may be localized to the palms, to the hands and feet or is generalized. *Acquired peeling of the palms* is the most common condition (keratolysis exfoliativa) and affects the palms of young adults in the summer months probably due to sweating. Lesions appear as tiny white rings or air bubbles, which soon rupture and peel off. Emollients and keratolytics are usually prescribed but are (not) very effective.

(1) العرقة الصيف

Keratolysis of the hands and feet (*Oudtshoorn disease*, keratolytic winter erythema) is a rare autosomal dominant disorder which may be precipitated by cold weather, febrile illness, stress and menses and improves by age. There is recurrent combined skin peeling of the hands and palmoplanter erythema. Histologically there is necrobiosis of the Malpighian layer and absence of the overlying granular layer through which the Malpighian layer is ejected. The disease begins at any age from infancy to early adult life. There is cyclical centrifugal peeling in the palms and soles and may spread to the dorsum of hands and feet and inter-digital spaces. Palmoplanter erythema develops and is followed by peeling which occurs in waves resulting in gyrate and polycyclic annular erythema which eventually resolves. Cycles repeat every few weeks and the palms and soles appear normal between attacks. There is (no) effective treatment.

(2) Peeling + Erythema (Waves + Polycyclic or Annular)

Generalized skin peeling occurs in the *familial peeling skin syndrome*. In this autosomal recessive syndrome there is a defect in profilaggrin and histologically the split exists at the corneal granular surface. Generalized superficial peeling starts at birth or in early childhood and is then persistent or periodic. Peeling is (not) preceded by fever or erythema, and can be produced by rubbing intact skin, especially if pre-soaked in water. Peeling sheets of stratum corneum spread across the trunk and limbs. The palms and soles are spared. Keratolytics and urea creams speed up shedding.

(3) لما بنبل وبلحسه بنزل قرف

(3)

Confluent and reticulate papillomatosis

Aetiology: There is strong evidence of an infective aetiology. The hyperkeratosis may present an abnormal response to microbial products. Response to several antibiotics supports a bacterial contribution.

Histopathology: Hyperkeratosis and papillomatosis are present without (acanthosis).

Clinical features: It occurs predominantly in (girls) beginning around puberty. Flat dry papules up to 5mm in diameter appear between the breasts and in the interscapular area. Neighbouring papules become confluent to form an irregular network. The lesions gradually extend over breasts and up and down the epigastrium and back.

- Girls at
- pub.
- dry brown pap. →
- Confluent → Network

Treatment: Various antibiotics may be effective and **minocycline** is mostly used. The response to antifungals is variable. Systemic or topical **retinoids** and topical **calcipotriol** may also be effective.

Theories :-

① Hormonal → DM, thyroid, obesity, pregn. (wt ↑↓)
② Hereditary (+ve F H)
③ Malassezia
Actinomycetes (Dietzia)

(7) Acral Acanthotic : in dark skin individuals
- at dorsal hands & feet specially the nuckles.

(8) Generalized : reported in children ē out Mg

تفسير مختلفين (9) Mixed Type : e.g obesity ass + Mg ass.
(10) Eruptive AN = IEMP

NB : Pseudo AN : refers to AN (Not) ass ē Mg
xx (لم يعد يستعمل اصطلاح ده حاليا)

Pathology : Hyperkeratosis + irregular spiky papillomatosis.
(No) Acanthosis + (No) Hyperpigm → so misnomer

Treatment:

1- The primary aim of treatment is to correct the underlying disease process. Often correcting the underlying cause results in resolution of the lesions.

- Correct hyperinsulinaemia through diet and medication
- Lose weight with obesity-associated AN
- Excise or treat underlying tumour
- Stop offending medicines in drug-induced AN

2- There is no specific treatment for AN. Treatments considered are used primarily to improve cosmetic appearance and include topical retinoids, dermabrasion and laser therapy.

(NB)

حالات كتيرة من AKF بيفتكرها اكوليت الـ Darier
Trunk lesions بتظهر قبل ← (الافتراض AKV) - Acral lesions of Darier

] it May be:
(1) Allelic form of Darier
(2) Form fruste of Darier.

Acrokeratosis verruciformis of Hopf (AD)

Aetiology: The lesions are typical of acral lesions in Darier's disease, but may occur as an isolated autosomal dominant trait. Mutations in the ATP2A2, the gene implicated in Darier's disease, have been found in acrokeratosis verruciformis.

Histopathology: Hyperkeratosis, acanthosis, and a prominent granular layer may be accompanied by papillomatosis and discrete pointed epidermal upgrowths said to resemble churche spires.

to diff from Darier:
(No) Acantholysis
(No) Dyskeratosis.

Clinical features: Flat or convex skin-coloured warty papules are present on the dorsa of the hands and feet, on the knees and elbows, and on the forearm. The condition occurs in both sexes and is usually present at birth or appears in early childhood. Nail lesions may suggest the diagnosis of Darier's disease. The condition resembles extensive plane warts and can be differentiated histopathologically.

Treatment: This is not satisfactory

(DD) ٣ مرضان
- Darier
- Plane Wart like lesions + TVC like lesion → (يعني ايه اسم المرض ده)
- Acrokeratosis Verruciformis.

DD of Plane extensive Wart like lesions in early life

داسوی

Follicular Keratotic disorders :-

(A-) Keratosis pilaris : (AD) Follicular Hyperkeratosis

Ch-By : Keratinous Follicular plugging (K.P Alba)

±

perifollicular Erythema (K.P rubra)

Types (1) Physiological [gooseflesh like] تشبه جلد الوزة

→ childhood - Adolescence

→ plugs ± ass ē hair retent^ or Twisting at Extensor limbs

→ Erythematous Component without plugging ± occur

± improved in summer & ē age

(2) Pathological :-

(i) Ichthyotic : ass ē

- → Icthyosis
- → AD الأكزيما
- → PC = Pachyonicia Congenita
- → Ectodermal dysplasia

"Follicular Atrophoderma" → (ii) Ass ē Atrophy:

- → K.p atrophicans (AD) Faciei (ulerythema ophryogenes) : Kp ē follicular atrophy at eyebrow & scalps
- → Atrophoderma Vermiculatum (?? AD) at cheeks & preauricular = atrophic worm eaten like. childhood (5-12 ys)
- → Folliculitis decalvans (??) (Scalp, ass. + eye) (XLR)
- → Keratosis Follicularis Spinulosa decalvans (See CIC Alopecia) Ass < PPK, eye, Amino acid

معروفة و مشهورة (iii) Erythromelanosis follicularis Faciei et Colli. 2nd decade

Bilat symmetrical

Δ of Erythema + Kp + Hyperpigm at < face, Neck

في الأطفال (iv) Lichen Spinulosus: Spiny follicular papules (ē)

xx Erythema, any Where

xx except face, Hands & Feet

Vit < A (<30 μg/dL), E, B deficiency ← (V) Phrynoderma : Horny plugs ē perifollicular papules at elbow, knee, kneck

(VI) Ker. circumscriptum.

Pityriasis Rotunda
(Pit. Circinata).

(2009)

Def: Asympt., Idiopathic dermatosis ch^ BY: Well defined, rounded, scaly pigmented patches.

Etiopathogenesis: Unknown but ±

1. Variant of Ichthyosis Vulgaris (because of same Histopath.)
2. Ass. with systemic dis:-
   - Malnutrition
   - MYcobact. inf. (TB & leprosy)
   - Mg (Gastric, hepatocellular & M.M)
   - liver Cirrhosis.
   - G6PD deficiency & favism

Epidemiology:
- Age: Usually (20-45 Ys).
- Sex: (No) predilect^
- Race:
  - Far east (اليابان، الصين)
  - Mediterranean basin (المغرب، ايطاليا، إسرائيل)
  - Africans, African-Americans.

CIP:
- Asymptomatic, non inflammatory, Well defined, large (10-30 Cm), circular & polycyclic scaly pigmented lesions usually on Trunk & extremities.
- NB: lesion may be surrounded by (Hypopigm halo or Totally Hypopigmented.
  - So there are 2 varieties: Hypo & Hyperpigm
  - Types: Hypo & Hyper / Type I & Type II

Types of Pit Rotunda
(Grimalt classification)

Type I	Type II
• Affect blacks & Asians. (Mg: السود)	• affect Caucasians. (القوقازيين)
• Age > 60 y.	• Age < 40 ys. +FH
• (-Ve) FH	→ (+Ve) FH
• Fewer lesions (<30)	• Multiple lesions (>30)
→ + May be ass. ē Systemic dis. or internal Mg.	- (No) ass. systemic dis or int. Mg.

- Histopathology: similar to Ichthyosis Vulgaris:
  (Hyperkeratosis + Hypogranulosis)
- DD: [T. Corporis, TVC] [Leprosy, Parapsoriasis]

Treatment (ليزر)

1 - Correction of underlying possible Ethology eg (Malnut. / Mg)
2 - Keratolytics & Emolients.
3 - Cs
4 - Retinoids (Topical & systemic)

---

5 **Flegel's dis.** = Hyperkeratosis lenticularis perstans (Mg)

- AD, appears at 30 - 40 ys.
- Etiopath: defective lamellar (odland bodies) granules (defective lipid content) → Hyperkeratosis.
- Clin: (1) at PP → pits (age)
  (2) profuse, disc or lens like hyperkeratotic papules at legs & calves ē irregular margins (cornflake sign)
- Removal of scales → easy Hge (DD: stucco keratosis (Hge, Papillomatosis))
- Hp: Hyperkeratosis, parakeratosis alternate ⟨ atrophy / Acanthosis (+)

DD

- stucco keratosis
  - difficult Hge
  - papillomatosis (Not atrophy)
- i) Parakeratosis
  - Hp ??
- ii) perforating
  central crust or plug.

Porokeratosis

Q (امتحان)

Def. Porokeratosis is a clonal disorder of keratinization characterized clinically by: annular hyperkeratotic papule or plaque, with a thread-like raised hyperkeratotic border; and histologically by "cornoid lamella".

- **Etiopathog:** KC Hyper proliferative disorder of unknown Etiology; ± related to:
  - 1- Inheritance: AD; (PM) Mibelli & PPPD.
  - 2- Immuno Supp.: PPPD ± d.t → Immuno Supp. / paraMg. & linear p (Mg)
  - 3- UVL (sun): DSAP.
  - 4- Mg: porok. is preMg ← قبل
- **Epidemiolgy:**
  - Age: childhood ↔ Familial / Linear → Adulthood
  - Sex: All (M) > F except DSAP (F > M). → other Types
  - Race: (Fair) >> dark (rare)

Types

1- Porokeratosis of Mibelli (PM)
2- Disseminated P. (DP)
3- Linear (LP)
4- Giant (GP)
5- PP

1- Porok. of Mibelli (classical Type)

- Papule/plaque(s)
  - single (but ± Multiple)
  - Asympt (but ± itchy)
  - Anywhere (but ++ at extremities)
  - Hyperkeratotic ē chic
- Both:
  - **Border:**
    - Well-defined, raised (Ridge), thready ē Thin-Central longitudinal furrows (Great Wall of China effect)
    - ± Verrucous
  - **Center:**
    - Atrophic
      - ± Hypo or Hyperpigm or
      - ↓ Anhidrotic & Hairless.

(Superf)

DSP = [2] Disseminated ± Porokeratosis: (Multiple lesions)

- Bilateral, symmetrical ē sparing → PP ✗, MM ✗
- SubTypes:

① Disseminated Superficial Actinic (DSAP)

at sun exposed areas specially legs

② Immunosupp ass: ← post transplant, HIV

③ HCV ass

④ Childhood (AD, 5-10ys)

(Mg) ass ← [3] Linear P: M=F, childhood, ē unilat. & Linear. Blaschkoid distrib. at limbs.

[4] Giant Porok.: - diameter >20 cm, Edge > 1cm
- at foot
- Highers Incid. of (Mg).

[5] Palmoplantar porok:- Multiple, Minute Hyperkeratotic papules ē minimally elevated border & With Atrophic center.

DD:-
- punctate ppk
- Wart

Types ← PPPD = Porok. palmaris et plantaris disseminata
Punctate porokeratosis of Mantoux

⑥ Syndromic porok.

HP → (edge) → Cornoid Lamella Type

Parakeratotic Cells:-
→ deeply Basophilic Pyknotic Nucleus.
→ Cytop. pink = Eos.

- Parakeratotic Column: extending from Keratotic in Vaginat° of epid.
- Granular layer → Absent ✗
- Spinous layer → Dyskeratotic ē Perinucl. Halo
- Dermis:- mild infilt.
  - dilated Capillaries
  - ± Amyloid.

- Center of lesion
  - Atrophic
  - → Hydropic degen.
  - Flattening of R
  - Amyloid depo

صدال أفضل edge

- NB: on Cornoid lamella

- Marked in P.Mibelli & less Marked in the other Types (Corresponding to the less elevated border in these Types)

- other dis. ē Cornoid lamella

- AK
- Warts
- Ichthyosis

All types of porok. undergo (Mg) (7-11)

Transformatn (BCC, SCC, Bowens) But

↑ Highest in Giant P. X No Mg in punctate porokeratosis of Mantaux

Treatment → NO ##

- sun-protectn
- Mg.

} الكلام على بالك صح

Trials: - Emollients
- Keratolytics
- Retinoids
- 5-FU
- Vit-D
- destructs: surgical or Co_2.

DD of PP Keratoses

2 Esp
- Punctate Keratoderma
- " Poroketatosis

3 Sup
- Spiny Keratoderma
- Spiny Hyperkeratosis (MMDH)
- PP filiform "

Spiny Keratoderma
VS
Spiny Hyperkeratosis
PP-filiform Hyperk

- others
  - Darier
  - Arsenical
  - Cowden

Myeloma → MM related specules

- MMDH = Spiny Hyperkeratosis

Et: ?
1- AD (early onset)
2- Trauma : sun, radioth.
3- drugs Cs, Etretinate

T-O-NT → - Mg : MM-related spicules ± Type of MMDH.

- CIP : Non-follicular spiny projections at trunk & extremities.

Hp: (3) Vacuities
- I: Parakeratotic Column (Cornoid lamella)
- II: orthokeratotic "
- III: porokeratotic Eccrine osteal & dermal duct Nevus (sweat duct Porokeratosis)

Tt
- Keratolytics
- Retinoids
- 5FU.

Spiny Keratoderma

- CIP: Firm PP Keratotic projections.

Et: ① familial (AD)
② Mg ass Cancer (lung, kidney, stomach), Leukemia, SCC, MM
③ Bg: Darker, Hyperlipidemia.

Hp: Parakeratotic Columns ē Hypogranulosis ((No) Dyskeratosis (May Vacuolar degen)

Cut Pseudolymphomas = Cut lymphoid Hyperplasia (CLH)

Def Heterogenous groups of disorders ch by mixed T & B cell lymphoproliferative process

mixed = Not Colonal

(Wake) clinically: (Bg)

Histologically: simulating Mg Lymphomas (So called Pseudolymphomas)

Classificatn: most cases of Pseudolymphomas (CLH) Contain mixed T & B Cells but one cell may predominate.

So: According to the predominant Cells can be classified into:-

- **Cut. B Cell Pseudolymphoma** (Lymphocytoma Cutis) — أكثر
- **Cut. T Cell Pseudolymphoma**

Aet

1. **Idiopathic**: most cases
2. **Reaction to**:
   - tatto & Acupuncture
   - Jewellery & Gold earring
   - Insect bite
   - Scabies (Nodular Scabies) (شفوي)
   - Trauma
   - Vaccinatn
   - Medicatn (Anticonvulsants)
   - Inf (Borrelia - H-pyloria - Molluscum, Folliculitis) — also HIV

1. Idiopathic (most)
2. Drugs (Anti Conv. Sp. phenytoin) → Drug induced PseudoL Synd.
3. Actinic Reticuloid (Pseudolymphomatous Actinic Reticuloid → at sunexposed)
4. APACHE — Now classified as (CTCL)
5. Jessner

(Types of Pseudolymphoma)

B-cell pseudolymphoma (Most cases)

(Lymphocytoma cutis) or (" adenosis Benigna Cutis)

Clinically

Age:
- Any (Common ≥ 3 & 4) but
- Borrelia → Childhood

Nodule (s) or papule
- Single or Few
- Asympt
- Soft doughy or firm (+++)
- Skin Colored, red-brown
- Scaly or crusted or No surface changes (+++)

Site
- Commonest → Face
- 2nd Common → chest & upper Extrem.
- Borrelia (chic sites) → Cold areas as (Nose, Ear lobe, Nipple, Areola & scrotum.)

Pathologically : simulating B cell Lymphoma (CBCL) = Lymphocytic Lymphoma

(وتقارن بين الاثنين جدول)

T cell pseudo lymphoma

2 Histological Varieties

① Band-like & perivascular infilt (Common)

- Clinically : MF like (DD not restricted to sunprotected areas as MF) + Solitary or fewer lesion
- Pathologically : as MF
  - Band like infilt.
  - ↓ [mild Epidermotropism (< MF)
  - ↑ [Marked spongiosis (> MF)
  - × [No Pautrier Microabscesses
  - ↙ [Acanthosis

MF وده الفرق بينها وبين

② Nodular Pattern (less Common)

Clinically : CBCL Like (B cell lymphoma like) = Nodules

Pathologically :-
- Nodular infilt of T cells
- × No Grenz Zone
- × No epidermotropism

Diff. bet CLH & Mg Lymphoma:

(Cuz most cases of CLH simulating B cell Lymphoma, the comparison will be bet. the 2)

CLH (Lymphocytoma cutis)	CBCL (Lymphocytic Lymphoma)
A · infiltration ch. BY: · Patterned (Nodular) فوقه · "Top heavy" · Grenz Zone ± · mixed infil. (Lymph (B+T), Neut, plasma cells) · Germinal follicles with → Mantle Zone, Tingible-body Macrophages	· Infilt. ch. BY: - Diffuse (Indian filling) شبه سلاسل الهنود - Buttom Heavy (deep dermis & s.c.t) - ± Grenz Zone - Lymphocytic infilt. (only B Lymphocytes) (Monoclonal) Mg: No → Germinal follicles, mantle zone, Tingible-body.
B · No Appendageal affection. XX	· Appendageal destruction.
C · Immunophenotyping: (polyclonal) · T & B Cells T · mixed CD4+ & CD8+ B → mixed Kappa & Lambda Expression - BcL-2 only on T Lymphocytes. ??	· Immunophenotyping: (Monoclonal) · uniform B Lymphocytes. نوع واحد بس - Restricted Kappa (or) Lambda Expression. - BCL-2 on Neoplastic B Cells (Some cases).
CIP · Solitary/few · children & adolesc. · ± Known Etiology	· Multiple · Adults · ??

NB:

(قشرة_غطاء) · **Mantle Zone:** Zone of (small) Lymphocytes cuffed (surround) around the Germinal follicles. ← حلقة حواليه (L)

· **Tingible body Macrophages:** Macrophages that engulf fragments of Lymphocyte nuclei (condensed chromatin). (CBCL)

NB: DD: "Idiopathic facial Aseptic granuloma"

Borrelia Pseudolymphoma (usually B cell):-

C
- children
- Cold areas < Nose / Ear also: Nipple, Areola, Scrotum (genitalia)

HX
- History of Tic bite.

sero
- (+Ve) Serum Antibs (Serology).

Drug induced Pseudolymphoma (usually T cell):

Called: Drug induced pseudolymphoma Synd.

- Commonest:
  - Phenytoin (تخيلي) → اهم واحد ع الاطلاق
  - Carbamazepine
- others: ⇐
  - Anticonvulsants
  - Antipsychotic
  - Antimalarial
  - ACE-I

(دكتوراة فقط)

- **APACHE**: "Acral Pseudolymphomatous Angiokeratoma of children"

قديما → Was originally thought as a Vascular Nevus but now proved as Pseudo-Lymphoma.

بس اسما → differs from other pseudolymphomas in:-

(acral) → ①. Favors Extremities (Acral)

(child) → ②- Age: 2-16 Ys

(angiokeratoma) → ③. (Unilat) grouped Red Violet Papules & Plaques (Angioma)

(DD) → - LA. Circumscriptum / - Verrucous Hemangio...

Cut. Lymphomas

- Hodgkins (rare)
- Non Hodgkins (Most Cut. Lymphomas are non Hodgkins)

Acc. to the origin

- Cut. T Cell Lymphomas (CTCL)
- Cut. B Cell Lymphomas (CBCL)

Can be classified Acc. to:

WHO & EORTC [European organisation for research & ttt of Cancer] into: 2 types (2005) (HL)

- Indolent (low grade, slowly growing) Mg.
  1. MF (65%)
  2. MF Variants:
     - Folliculotropic MF.
     - Pagetoid Reticulosis.
     - Granulomatous slack skin
  3. CD30 +Ve:
     - Lymphomatoid papulosis
     - Anaplastic Large.
  4. S.C panniculitis Like (CD3+, CD4-, CD8-, CD56-)
  5. CD4 small/medium pleomorphic (CD3+, CD4+, CD56-, CD8-)
- Aggressive
  1. Sezary Synd
  2. Adult T cell / Leukemia / Lymphoma
  3. CD8: Aggressive Epidermotropic
  4. NK/T: Nasal Type (destructive, mid facial & Trunk ulcerating)
     - EBV
     - Leishm. or Paraneoplastic
  5. γ/δ T
  6. Peripheral TCL (NOS)

تصنيفات أخرى

(65%) MF Sezary	احفظ ملخص لبعض أهم نوعية CTCL
(25%) CD30+	Indolent: MF, MF Variant, CD30+ LYP
(10%) باقي التصنيف	Aggressive: Sezary, CD8 CTCL Aggressive.

Treatment of CLH

1- Remove the cause → Drugs / Insect

2- Cs → Topical / Intralesional-

3- surgical EXCision.

4- Radiotherapy.

5- Antimalarial.

6- PDT.

MF (MYCosis Fungoides) (updated 2013)

(لم يأت في الامتحان)

(Alibert-Bazin Type)

Def → Commonest Type of CTCL (65%) thats has Indolent course d.t Mg prolif of CD4.

- AET → unknown but ± d.t:
  - Genetic (Genotraumatic T cell prolif) [Genetic Instability → clonal prolif]
  - Infection < H. pylori, Borrelia, HTLV1
  - Immunological (Th2 profile, ↓ CD8)
    - Th2 profile → [↑ IL 4, 8, 6, 10]
    - ↓ CD8 → (↓ IFN-γ)

- **Epidemiology**
  - Age: Any, but commonest around (50 ys)
  - Sex (M) > F
  - incid: (0.5 / 100,000) (٥ حالات كل مليون حالة) "غريبة !!"

- C/P
  3 stages [Site < Covered areas of trunk, buttocks] مكان مميز

[1] Patch stage
↓
- Ecz. or psoriasis like
  Sometimes with atrophy or Poikiloderma.
- Pathology: Non specific

So it is:
- Clinically: non specific
- Pathologically: non specific
- So How to suspect ??

ECZ. shows
1. persistent itching despite of adequate tt of ECZ. بالرغم
2. Reticulation.
3. Vivid Coloration (لونه احمر وشديد)
4. bizarre configuration

Biopsy ← لو ما خفتش ب Topical

[2] plaque stage
↓
- Eczema or Psoriasis like
+
- Sometimes with Arciform, Annular or Polycyclic Pattern.

[3] Tm stage (Mycotic stage)
Large, Nodules & plaques that may ulcerate.

> **NB** A fourth stage may be described:
> **[4] Erythrodermic stage** (Erythrodermic MF)

- Each stage may have many clinical varieties

- Patch stage
  - P
    - Parapsoriasis.
    - PAV = Poikiloderma atrophicans Vasculare.
  - H
    - Hyperpigmented
    - Hypopigmented (
    - Hyperkeratotic (verrucous)
  - B
    - Vesicular
    - Bullous (on either NL skin or on Top of MF lesions)
    - pustular.
    - vasculitis-like & purpuric
  - Follicular. (ay)

- Plaque stage.
  - Coalescence of multiple plaque
  - Annular, Geographic or Arciform pattern of areas of NL skin (islands)
  - Central depression may occur

- Tm st
  - Tm dem
  - Tm develo de novo
  - Patch

- Erythrodermic MF (Not Sezary)
  - Mucosal
  - Syringotropic (Lymphoid Hyperplasia)

NB: other similar Classification :-

1- premycotic stage (Patch / plaque stage)
2- Mycotic stage (Tm stage)

Sc: MF is considered as "Great Imitator" as it may be presented by any picture

Q (شفوي) Great Imitators in Dermatology :- تجيب بأي صورة

- MF
- Sarcoidosis
- $
- Leprosy
- Scabies
- Drug Erupto

- Cause of Death
  - Systemic involvement.
  - Immunosuppression → opportunistic Inf.

Classificat^ of MF (MF & SS)

T (Tm)
- 0 → lesion is suspicious clinically &/or pathologically
- 1 → localized patch / plaque < 10% BSA
- 2 → Generalized " " > 10% BSA
- 3 → Tm (Mycotic)
- 4 → Erythroderma.

N (L.N)
- 0 → No L.N
- 1 → clinically: Enlarged / Pathologically: Free
- 2 → clinically: Enlarged / Pathologically: involved (but) without Effacement.
- 3: → as 2 + Architecture effacement.

M (Meta-stasis)
- 0 → No visceral affect^
- 1 → Visceral affection.

B (Blood)
- 0 → 0 - <5% Sezary Cells
- 1 → >5% (or <1000 cell) Sezary Cells. 5-19
- 2 → ≥ 1000 /ml L > Sezary Cells + +Ve clone.

0 & 1 "Sezary phenomenon" (15%)

only Mg cell في architicture عليم زي الطبيعي

(Imp. Mg) **Staging** (طريقتين) (Ref. (# of skin dis. 2012) (Emed. 2013)

A. 1st Method

• Stage 1:
- A: patched plaques < 10% BSA. (T_1)
- B: " 1 " > 10% " (T_2)

• Stage 2: as stage 1 +
- A: Non Mg L.N (clinically ↑↑ / HP: - Ve = Dermatopathic) (N_1)
- B: cut. Tm (Mycotic stage). (T_3)

• Stage 3: → Erythroderma. (T_4)

• Stage 4:
- A_1: Erythroderma (T_4) + Blood (B) involvement
- A_2: Mg Nodal ± Total effacement (N_3)
- B: Visceral InVolVement (Lung, Liver, BM). (M_1)

B. 2nd Method (TNM)

Invs for MF

(Rel skin dis. 2L)

(HL) deletion in Suppressor Genes

(IV) Genetic Testing ← Advanced IE

- pTEN deletion on Chromsone 10q

(1) Skin Biopsy: for 3

(i) Histopathology (HP)

(ii) Immunophenotyping

(iii) T-cell Receptor (TCR) Gene analysis

(2) L.N Biopsy (if enlarged) → HP, Immunophenotyping, TCR Gene Analysis

(3) Visceral:-

- Blood: → Sezary Cell Count (Buffy coat smear), Immunophenotyping (by flowcytometry) → صعوبة فرق الى موجود بالكبد
- Liver: LFTs, LDH (+), Uric acid. → markers of Bulky & Aggressive MF.
- RFTs.
- CT (thorax, abd, pelvis) if stage ≥ 2A → enlarged LN
- BMA (if +ve Sezary or Hemat abnormalities)

(4) HTLV-1 Serology: as a causative Virus.

- Immunophenotyping: (Flow cytometry)

Pan-T Cell Markers
- CD2
- CD3
- CD5

- classically:
  - CD3+, CD4+
  - CD7-, CD8-, CD26-

- Rarely (Aberrant Expression):
  - CD4-, CD8+ (CD8 → CD7)
  - CD4-, CD8-
  - CD8+ (Hypopigmented MF)

- TCR-Gene analysis: (PCR & SB)

T-cell receptor (TCR) gene analysis consists of analysis of DNA from tissue samples for the detection of clonal rearrangements of the TCR genes as a marker of a monoclonal T-cell population. Analysis of TCR genes in MF is now a standard approach that has diagnostic, prognostic and therapeutic implications. Studies are based on sensitive PCR techniques. T-cell clones can be detected in 70% of patients with early stage MF and are almost invariable in patients with later stages of the disease.

The underlying molecular pathogenesis of MF is currently unknown. No disease-specific translocations have been identified, but various abnormalities of tumor-suppressor genes have been detected including overexpression and mutation of p53 in advanced stages of disease. Inactivation of both p15 and p16 genes has also been detected. Frequent allelic losses on 10q have been detected predominantly in late stages of the disease. A specific pattern of chromosomal losses and gains has also been found in MF.

((يحفظ جيداً))

Pathology of MF

(infilt. of) → Epid → Epidermotropism
Dermis → Lichenoid

Epidermis

- **Epidermotropism**: Epidermal infilt by atypical Mg. Lymphocytes (MF cells or Lutzner cells) that residing in Basal Cell Layer or st. spinosum singly or in groups called **Pautrier Microabscesses** (Nests) surrounded by clear Halo
+
Scanty spongiosis

MF or Lutzner Cells = Mg T cells ē:
- Convoluted
- Cribriform
- Hyperchromatic

(Nuclei)

شكلها ايه !؟

Dermis

ده المستحيل الأول

Band-like inflamm. Infiltrate (Lichenoid) Composed of Mg (MF or Lutzner) Lymphocytes

مهم

Epidermotropism ē MF Cells ē Scanty Spongiosis & Pautreir Microabs + lichenoid infilt

- in Patch stage: Non specific band like infilt ē Histiocytes + Lymphocytes + few epidermot.
- Plaque stage: واضحة جداً
- Tm stage: dermal infilt → diffuse; Epidermotrop → -ve

NB: **Epidermotropism**: Epid infilt by ↑ cells (Mg cells) → Lymphocytes, Pagets, Pagetoid

- infilt by (Mg) T-Cells usually ass. ē ↓ Scanty Spongiosis → MF
- infilt by (Bg) T cells + Marked ↑ spongiosis [≡ Exocytosis] → Inflammatory Condit.s eg Eczema

الملخص المهم

Treatment of MF

Stage 1 = T_1 / T_2

- **1st line** (SPT)
  - Topical Cs
  - Emollients
  - Topical chemotherapy
  - UVB or PUVA
    - ممنوع قبل ١٦ سنة
- **2nd line**
  - RePUVA < PUVA / Retinoids
  - IFNα2a
  - TSEB
  - oral bexarotene

Stage 2 — As 1 + (A → N_1 / B → T_3)

- **1st line**
  - IFN-α2a
  - Local radiotherapy
- **2nd line**
  - MTX
  - Bexarotene (oral)

Stage 3 = T_4

- **1st line**
  - IFN-α2a
  - MTX (low dose)
  - ECP = extracorporeal photopharesis
  - PUVA
- **2nd line** (as stage 2+)
  - TSEB
  - Bexarotene
  - LN radioth.

Stage 4

- A_1 = T_4 + B
- A_2 = N_3
- B = M_1

- **1st line**
  - as stage $\leq \frac{1}{2}$
  - + Combination Chemotherapy or L.N radioth.
- **2nd line**
  - Purine-analogues
  - Bexarotene
  - DAB-IL2 (DAB = Diphtherial toxin + IL2)

الملخص المهم

* Stage I (Skin directed ttt)	* Stage II	* stage III: as II+	* stage IV
• Topical (Cs, Chemoth., Emollients, Bexarotene gel, Ni Mustard or Mechlorethamine (Valchlor)® gel → FDA) • PUVA • RePUVA	• IFNα2a • Bexarotene • MTX • Local Radio (2013)	• ECP ± PUVA • TSEB • LN radioth.	as I & II+ • Combination chemotherapy or L.N radio • Bexarotene • DAB-IL2

(i) • **Topical chemotherapy** (stages I & II)

- **Nitrogen Mustard**: 10 mg in 60 ml Water or as oint
- **Carmustan** (BCNO).

S.E
- BM--
- 2ry Mg

(ii) • **IFN-α2a**: 3 min. IV X3 /W → 6 mns resp → For 1-1.5 Ys • Mech. < ± cytotoxic T cells.

- *Toxin therapies*: Denileukin Diftifox (Onzar) is a fusion of diphtheria toxin and IL-2. It is capable of inhibiting protein synthesis in tumor cells expressing high levels of the IL-2 receptor, resulting in cell death. It is given intravenously as (18 µg/kg/day) for 5 days, repeated every 21 days for 4-8 cycles. Adverse effects include fever, chills, myalgia, nausea and vomiting. Acute hypersensitivity reactions occur in 60% of patients. The response rate is 30% in stage IB – IVA. It may be useful in advanced cases.

18 µg/kg/d
(IV) 5d/1w
for 5 cycles

- Retinoids For MF:-

① Isotretinoin → effective specially @ PUVA (RepuVA)

② Bexarotene:-
- Act on RXR → promotes Mg cells apoptosis.
- 2 Types

Topical 1% gel
- FDA for refractory or persistent MF
(IA - IIA)
- SE irritat^

Systemic (Oral) ← Sezary & refractory MF
- Dose: 300 mg/m² ld for 4 ms
- S-E - Hyperlipidemia ((TTGs)) ↑
- Hypothyroidism-

- Chemotherapy:-

Single agent → Deoxycoformycin
Multiple " → CHOP
- Cyclophosphamide
- Hydroxy daunomycin
- oncovin
- Prednisone-

→ Recent Hit for MF:-
↓
Autologous BM Transplant^
(or)
Allogenic stem cell "

② Folliculotropic MF (Alopecia Mucinosa)

- Erythematous, Indurated or Gelatinous plaques & follicular papules ch BY:-
  - (i) Alopecia (±)
  - (ii) Severe "itching"
  - (iii) Mucinorrhoea
- (at) Head, Neck, scalp.

2 Types:-
- inflammatory (Bg)
- MF Associated
  1. 1ry (acute < chr)
  2. 2ry (15%)
  3. Urticarial like

(Imp) - Any Alopecia Mucinosa in pt > 40 yrs; it may be a Follicular MF or will develop = MF (Sg) → Biopsy

Histopath: Mucin Infilt. + folliculotropism of Hair follicles

Prognosis: Bad, corresponds to stage IIB MF = T_3

Hx:
- Inflammatory: Dapsone or spt. Cs
- Mg type

Hx: Need Aggressive Hx

③ Pagetoid Reticulosis (Sep.) → "Localized Acral MF" (ch BY)

NB P. Reticulosis:
1. Localized: Woringer Kolopp dis
2. Generalized: Kettron Goodman dis

- chr. localized < Patch(es) / Plaque(s) (usually) Acral
- long duration
- slow progression
- (Bg) course ((No) Extra cut. affects & death)

Pathology

Purely Epidermal (NB: Reticulosis: ↑ Infilt of Cells derived From Monocytes)

Epidermis < Hyperplastic Epidermotropism: by Pagetoid Haloed Lymphoid Cells (Pagetoid Cells (large, sized, cribriform Hyperchromatic Nuclei & Abundant Vacuolated Cytop. in Nests or single). surr. By halo Pale)

(Free) ← Dermis: small Lymphocytes infilt. (No Mg cells) + Histiocytes

Immunophenotyping: → $CD3^+, CD4^+, CD8^-$ (or) $CD3^+, CD4^-, CD8^+$

lax skin

④ Granulomatous Slack skin (Redundant)

DD (lax skin):
- (i) PXE
- (ii) Cutis laxa

- Rare Indolent Variant ch BY Pendulous lax Atrophic folds at axilla & grion
- Path: Granulomatous infilt. ← ± Ass c MF

Clonal T Cells: $CD3^+$ $CD4^+$ $CD8^-$

⑤ Lymphomatoid Papulosis

(2014) (low grade CTCL)
CD 30 +ve CTCL

Def Chr., Recurrent, self healing, Cut disorder that
(ms → 40Ys)
- Clinically: → (Bg)
- Histologically → resemble [CD30 +ve Mg Lymphoma] (Ki-1)

Incid of Ass. Mg Lymphoma: (5-20 %) usually (following) appearance of Ly.p by upto 20Ys (but may occur Before or with same time of Ly

Commonest Tms: may develop from Ly-p.
يتحول لنوع منهم
1. CD30 +ve (Anaplastic large cell Lymphoma (ALCL) =
2. MF
3. Hodgkin's.

NB:
- old classifications: is that Ly-p (is) T cell Pseudolymphoma
- Recently: Low grade Mg CTCL (CD30+)

C/P: → ① PLEVA like.

(Age: any but +++ >50Ys)

مش مهم differ from it in
1. Larger (كبير) — lesions
2. Fewer (قليل) — lesions
3. ↑ tendency for Necrosis

- Recurrent Crops of red papules (≃1cm) → papulo vesicular, papulo pustular, or Hgic then → Necrotic papules 2-8Ws → Spontaneous resolution ē Varioliform Hypo or Hyperpigmented Scars → "Recurrent"
- [Site]: any, but Commonest is the Trunk & Extremities
- [usually]: asymptomatic ✓

② Nodular or plaque Type: ↑ suspicion of Mg Lymphoma so (Called) → [Border line Ly-p]

Histopathology

↓

- Mixed dermal infilt
  - Lymphocytes (atypical)
  - Neut (LEN)
  - Eos
  - free red cells
- $\bar{w}$ ±
  - Wedge shapped ▽
  - or
  - band like & perivascular (MF like)

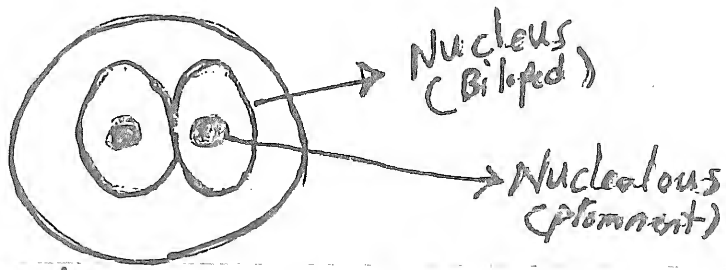
{ wedge ▽
band - - - - -
peri vasc }

- there are 3 Types of Pathology According to the predominant T. cells (CD . size .. like) epidermotri

• Type A (Histiocytic) يتحول → Hodgikin

↓

Large Reed - Sternberg like cells (CD30 +ve $\bar{c}$ bilobed Nucleus & prominent Nucleolus)



← oWel's Eye or Mirror Image Nucleus.

- Epidermotropism (+/-)

• Type B (Lymphocytic)

Small (MF) like cells (CD30 −)

(++)

• Type C (CAlcl)

large CD30 + (anaplastic) T. Cell Lymphoma like cells.

• Treatment

(Lymphoma) {
- مش مهم العلاج لانه مش هايمنع حدوثه
- Aggressive ### عشان نمنع حدوثه

⊙ هدرسين

↓

⊙ Most effective → **MTX**

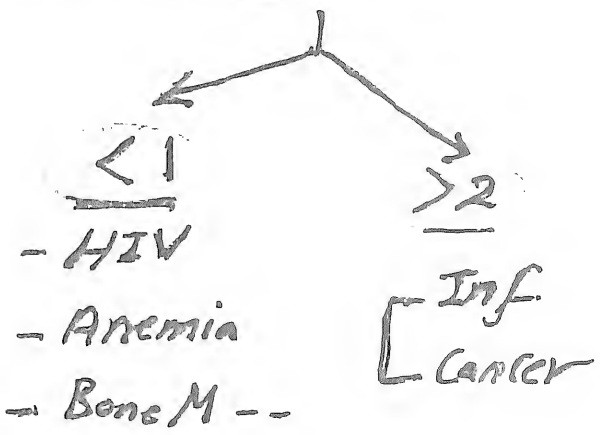
⊙ others : Dapsone, Cs, phototherapy, Aldara, IFN, Brentuximab (Anti CD30)

- CD30+
  - Transmemb. protein of TNF family
  - Expressed in = Lyp, ATCL, HD, MF

- Dermoscopy of Lyp → Emedicine.

NB

- CD4 : 500 - 1500 /mm³
- CD8 : 150 - 1000
- CD4/CD8 ≃ 2



Histopathology

↓

3 Histological Varieties

1- Type A (Commonest 75%) & commonest To develop Lymphoma

Infiltrate

- Wedge shapped
- mix of:
  - Large atypical Lymphocytes
  - Small Lymphocytes
  - Neutrophils
  - Eosinophils
- Exocytosis (epidermotropism ± spongiosis)

Atypical Lymphocytes

↓

Large Atypical CD30 +Ve Reed-sternberg like

Mirror Image → (multinucleated or ± bilobed Nucleus ± prominent Nucleulous) (Owel's Eye)

↓

Inclusion like Nuccoli

2- Type B (similar to MF)

Infiltrate

band like & peri-vascular infilt. (MF like)

Atypical Lymphocytes

(Small-medium sized) CD30- MF like (Lutzner) cells

3- Type C (Similar to ALCL)

Infiltrate

Few infiltrate

Atypical Lymphocytes

Large Atypical CD30 +Ve cells

(Treatment)

** - may be (not) necessary (doesn't prevent occurance of Lymphoma)

So ttt indicated when there are symptoms & when there is Risk of complications

- Superpotent Cs
- PUVA
- BCNU
- MTX

Sezary Syndrome (SS)

Def: Aggressive Type of CTCL ch BY Triad of:

clinically Δ of:

- Generalized Erythroderma
- L.N
  - Usually: cervical, inguinal & axillae
- Leukemia
  - (Mg Lymphocytes = Sezary cells in Blood)
  - Absolute Number > 1000 / uL
  - [B2 stage]

B2 st

- @Skin: Generalized Erythema & Scaling = (2) Lichenification, Leonine face
- ⊙ Hair: Alopecia
- ⊙ Nail: dystrophic
- ⊙ Eye: oedema & Ectropion
- ⊙ P.P: Hyperkeratosis of Palms & soles

لأنه الجلد بيتقشر

Symptoms
1. pruritus (severe)
2. Burning
3. Perspiration

دكتورة..

According to the international Society of Lymphoma: ≥ 1 criteria of the following is diagnostic:

1. Absolute Sezary cells > 1000/uL
2. Lymphocytosis & +ve Clone in Blood
3. Immunophenotyping shows a any:
   - i. CD4:CD8 > 10
   - ii. Aberrant expression of Pan-T cell antigen: loss of any: CD3, CD2, CD4, CD5, CD7
   - iii. loss of Both CD4 & CD5.

onset
1. as Sezary from the start
2. as MF then Sezary (±)

SS Δ ← Erythroderma, L.N, Sezary Cells > 1000.

NB Sezary phenomenon - presence of sezary cells in No < 1000 (<15% conc.) & in conditions others than

@s:-
1. NL individuals
2. Ps
3. Paraps
4. CTCL
5. CBCL
6. Lyl

→ "Erythrodermic MF"

- BCC
- DLE
- L.P

PreSezary Synd

↓

Non Specific Erythroderma
+
Few Sezary Cells < 15% (< 1000)
that may <u>progress to SS</u> تحول

*** Path. of SS** (purely dermal) as MF but differ in:
- (-Ve) Epidermotropism (Free)
- Monotonous Cell infilt (dermal & (L.N) ē effacement)

Treatment :-

(1-) ECP (Rx of choice; others → MTX, Retinoids, IFNα2)

Rx Triad

(2-) Antibiotics (staph. is a leading cause of death)

(3) Antipruritic (sever itching)

Classificat^n of Erythrodermic CTCL:

ماهو الفرق بينهم ؟؟
(i) Sezary Erythroderma
&
(ii) Erythrodermic MF

Types	preexisting MF	Blood
1- Sezary	- Rare ±	→ Leukemia B2 ✓✓
2- Erythrodermic MF →	- Always (++) ✓✓	Bo - B1
3- Erythrodermic CTCL; Not otherwise specified.	- Absent --	Bo - B1

5 ys Survival Rate in CTCL
→ MF & Follicular Mucinosis (88% & 80%)
→ Pagetoid Ret, Granulom-slack skin & LyP, ALCL (100%) → Sezary (24%)
أسوء ←

Cut. BCL
- FCL : 99%
- MZL : 95%
- DLBCL : 50-85 (Leg أسوء > Intravascular)

ECP

سؤال امتحان

Extracorporeal photopheresis

Emed 2014, Bologna)

(extracorporeal photochemotherapy)

→ Type of photochemotherapy

- Performed using the UVAR XTS Photopheresis System developed by THERAKOS©, a Johnson & Johnson company.
- The Session involves 3 steps and takes about 3 to 4 hours to complete.

- Steps : -

1- step 1: Leukapheresis

"5-10 % of pt WBCs"

This involves intravenously drawing the patient's blood (225ml) is passed through 3 cycles of leukapheresis) and separating out and collecting the white blood cells (WBCs) before the rest of the blood is re-infused back into the patient.

2- step 2: Photoactivation

The collected WBCs are mixed with psoralen, which makes the T-lymphocyte cells more sensitive to UVA radiation. The treated WBCs are then exposed to UVA.

NB
① oral psoralen
Now: local addition of Ps

3- step 3: Re-infusion: The treated WBCs are re-infused back into the patient.

Mechanism of action: unknown but may be due to:

1. Selective Apoptosis of Abnl T-Cells (غير منطقي نظراً لقلة عدد الـ WBCs المتأثرة)
2. Immune Tolerance: ↑ Treg cells (CD4, CD25, foxp3) → (--) Effector T cells & (--) APCs.
3. ↓ products of proinflammatory cytokines (IL12 & TNFα).

الأنواع

ادخل تاني

Side effects of ECP?

- S.E
  1. Fever
  2. Rash
  - Hypotension & Tachycardi.
  - Anemia
  - Thrombocytopenia
  - photosensitivity
- C.I
  - Aphakia (عدسة العين)
  - Anemia
  - Thrombocytopenia (heparin Induced)
  - Pregnancy
  - Hypersensitivity
  - Cardiac dysf.
- precautions
  (i). وقف علاج الضغط
  (ii) تعليق الهيبارين
- Criteria of success in MFI Sezary :-
  (i) CD4 : CD8 < 10
  (ii) low LDH
  (iii) WBCs < 20,000
  (iv) No L.N or Viscera

جلستين على يومين متتاليين كل ٢-٤ أسابيع لمدة ٣-٦ أشهر ... (CTCL)

(الجلسة ٣-٤ ساعات)

Indications :-

- M.S
- PV
- SSC
- GVHD
- Transplantation
- CTCL (MF) (FDA) (1988)
- HIV
- SLE
- EBA

(D. Essential ??
updated (2014)

Parapsoriasis

Def: groups of papulosq. skin disorders that resemble psoriasis clinically but without specific Histopath.

NB: - Because of the variation in clinical presentation and a lack of a specific diagnostic finding on histopathology, a uniformly accepted definition of parapsoriasis remains lacking.

Classification (Types): (Brocq; 1902)

1- Small plaque parapsoriasis [Digitate dermatosis, chr. superficial scaly dermatitis]
2- Large " " [Ps en plaque]
3- pityriasis Lichenoides (Acuta & chronica)

• Small & Large plaque para ps.
(Parapsoriasis en Plaques)

Etiopathogenesis both disorders are (Dermatitis) ch BY superficial cut. lymphoid infiltrate Composed primarily of (CD4+ T cells) this dermatitis ±:

- +ve clonality / Atypical / atypical
  - Polyclona → Small plaque paraps → So (No) progression to MF (reactive process)
  - Clonal → Large plaque paraps → So it may progress to (MF) (if)
    - (No) atypical Lymphocytes → still paraps (preMF)
    - atypical Lymphocytes → if is MF

Epidemiology:

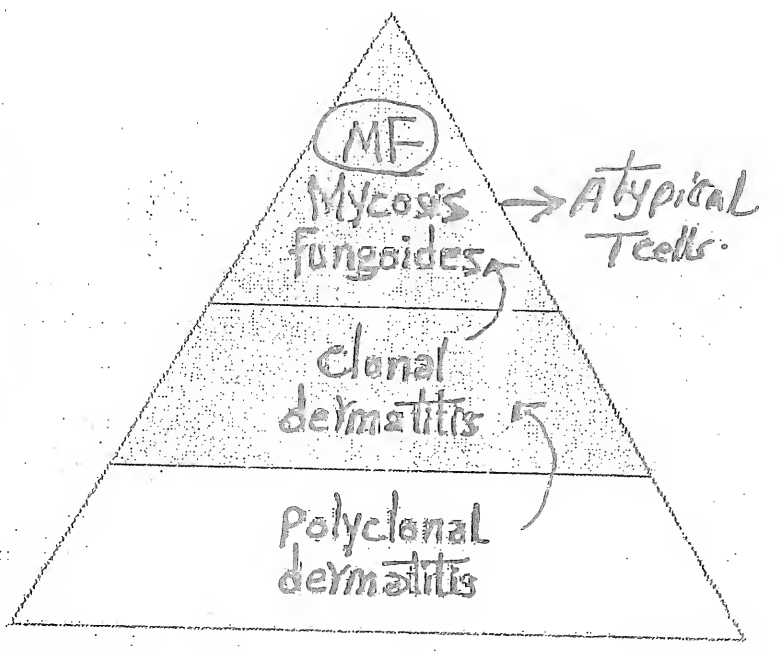
Age ~ (50ys)

Sex: (M) > F (3:1)

- So **Clonal Dermatitis** can be defined as: lymphoproliferative disorders that may constitute an intermediate or Transitional step bet. chr dermatitis & overt CTCL.
- So **MF pyramid** can be envisioned in ⓦ Some cases evolve from the large No of chr dermatitis cases through the intermediate stage, clonal dermatitis.

THE MYCOSIS FUNGOIDES PYRAMID AND THE PROPOSED TRANSITIONAL ROLE OF CLONAL DERMATITIS IN THE EVOLUTION OF MYCOSIS FUNGOIDES

Clonality	Pathology
clonal →	Mycosis fungoides
clonal →	Dermatitis
Polyclonal →	Dermatitis



- C/P of Para psoriasis ✓

Asymptomatic (or mildly pruritic), chr, slightly scaly, light salmon colored oval or rounded patches (± plaques) on Trunk & Extremities ✓ ✓

In:

- Small plaque Type:
  - patch < 5 cm. diameter. (> 10cm ضد التفكك)
  - Variants:
    1- Digitate type: Elongated, finger like patches on Trunk. صوابع ك.
    2- Xanthoerythroderma pestans:- the patches surr by yellow hue. لون
  - Fate: Spont remission within ms-ys. (rare progression to MF). نادر لو حد

- Large plaque
  - patch > 5 cm with (atrophic, cigrette paper ورقة السجارة or Tissue paper, wrinkling)
  - Quality
  - Variants:-
    1. Poikilodermatous Type
    2. Retiform Type: Network or Zebra stripe like
  - Fate: remission ⓔ ttt or progress to MF (No Spont resolution)

23

(90)

NB:- Incidence of progression to MF:

- in small plaque P : → rare.
- in large " " : → (10%) / decade.

Acfetman expressed that Large plaque Type is MF

Histopathology :

- (1)- small plaque parasps : → mild non specific spongiotic " polyc dermatitis & parakeratosis + superficial perivasc Lymphoid inf
  - Spong
  - Parak
  - perivasc
- (2)- Large plaque " : → as above & there may be lichenoid Lymphocytic infiltt. (No spongiosis)

→ the predominant cells are CD4 T cells ē " clonal "

(+Ve) clonality in Large Type & (-Ve) clonality in small type)

• DD :-

PRINCIPAL DIFFERENTIAL DIAGNOSIS OF SMALL PLAQUE PARAPSORIASIS AND LARGE PLAQUE PARAPSORIASIS	
Small plaque parapsoriasis	**Large plaque parapsoriasis**
– Pityriasis rosea pit rosea	– Mycosis fungoides MF
– Drug eruption, in particular pityriasis rosea-like	– Drug eruption, in particular mycosis fungoides-like
– Pityriasis lichenoides chronica PLC	– Psoriasis Ps
– Psoriasis Ps	– Poikilodermatous autoimmune connective tissue diseases AICTDs
– Mycosis fungoides MF	– Poikilodermatous genodermatoses
– Nummular dermatitis ND	– Chronic radiodermatitis
– Secondary syphilis S	

Treatment

- small type → assurance about Bg Nature
- Large type : → should be treated ↓ to avoid MF.

THERAPEUTIC LADDER FOR SMALL PLAQUE PARAPSORIASIS AND LARGE PLAQUE PARAPSORIASIS	
(3) Topical corticosteroids (2)	
Topical tacrolimus (3)	
Topical coal tar products (3)	
(3) Sunlight (2)	
UVB (2)	
PUVA (2)	
(3) Topical bexarotene (2)	
Topical mechlorethamine[*] (2)	
Topical carmustine[*] (2)	
(1) → Antihistamines[†] (3)	

Both → Follow up.

NB : in Both types : Follow up Every 6ms (Large type) / 12ms (Small ")

if ↑↑ : size, No, Atrophy, in durat → Biopsy ?? MF.

Pityriasis Lichenoides

Essential 22 (2014)

Def: T cell Lymphoproliferative disorder of unknown Etiology

Etiopathogenesis: (3,2 مش مهم)

- Unknown but there are 3 theories.

(1.) Hypersensitivity reaction to foreign antigen as drugs or infection: eg

- Toxoplasma Gondii
- EBV.
- CMV.
- HIV.

- staph or strept.

(2.) T-cell lymphoproliferative disorders with lesional T cell infiltrate of the following Types:-

- CD8+, CD30+ (ki-1) → in (PLEVA)
- CD4+, CD7- → in (PLC)

Most Accepted ← (2.)

(Relatively Bg form of CTCL)

NB:

(3) Immune-Complex Vasculitis

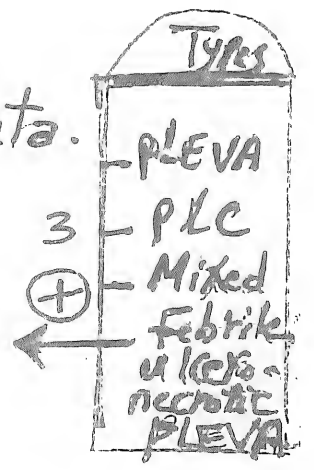
Classification (Types) of PL:

"Mucha-Huberman dis"

(1-) PLEVA: Pit Lichenoides et Varioliformis Acuta.

(2-) PLC " " chronica.

(3-) Mixed PL (PLEVA + PLC lesions)



⊙ Epidemiology: • Age: usually affect children (3-15 Ys)
(للإصابة تبدأ في أول ٣ سنة من العمر)
• Sex: (M>F)
• Race: (No) predilection

CIP of PLC

PLEVA
(Abrupt) onset of Asympt. (or pruritic burning) Erythem-atous papulo-vesicular lesions → rapidly progress to Hyic Vesicle → crustat^n → ulcerat^n
Healing → Variolaform scars.

PLC
(gradual (6 Ver days - Ws) onset of asympt. Erythematous-red brown lichenoid papules ± fine scaling (Frosted glass like)
Healing → Hypo → hyperpigm. (Hypo > Hyper)
NB: lesion ± polymorphic (lesions at different stages of Evolut^n).

Mixed PL
Polymorphic lesions ± mixed PLEVA & PLC picture.

Mica Scales (كاشف الحمل تطلع قشرة واضحة زي قشرة العدس)

Site: lesions usally located at Trunk, buttocks & proximal Extremities.

Course: PLEVA → resolve within Ws ± pox like scars [Variolaform]
PLC → chr ± exacerbat^ & remission. "Post Hypopigm. is Very Common"

NB (1-) PLEVA may evolve into PLC
(2-) ulceronecrotic PLEVA is variant from PLEVA
ch^ BY: Necrotic ulcerating lesion + Marked Constitutional Manifs.
(3-) Some studies have suggested that the distribut^ of the lesion is more important than their acute or chr Nature in predicting the outcome:-
- Diffuse distrib^: shortest course (≃ 11 ms)
- Peripheral " : longest " (≃ 33 ms)
- Central " : Intermediate

Constitutional Sympt + death

NB ⊙ Febrile ulceronecrotic Mucha-Habermann dis:- موكا هوبرمان

- subtype of PLEVA ← Hypersens. to Inf / T-cell prolif dis. / T-cell dyscrasia = hyperplasia
- differs from PLEVA in:-
  1. the Necrotic papules develop:
     - ulcers: large & crusted.
     - Hgic blisters
     - pustules
  2. Very painful مؤلم
  3. systemic manif
     - Fever
     - Sore throat
     - Abd. pain & diarrhoea
     - CNS & Lung affection
     - splenomegaly
     - arthritis
     - Sepsis
     - Anemia
  4. death may occur ✓

Tt
1. Tetracyclines.
2. Immunosuppressives + Tetracyclines ± Antivirals

DD

PLEVA	PLC
- LyP	Guttate ps
EM	PR
DH	$
- Arthropode bite	L.P

HP

- PLC
  - Focal parakeratosis
  - NL granular layer
  - disappearance of DEJ
  - Superficial dermal infilt.

- PLEVA
  - Confluent parakeratosis.
  - Hypogranulosis.
  - VID ē intravascular lymphocytes (Necrosis, kcs, Ballooning)
  - ⊙ Dermal:-
    - Edema
    - Wedge infilt. (superficial & deep lymphohistiocytic)
    - Intravascular margination of Neutrophils.
    - RBCs extravasation.
    - Vasculitis

⊙ Not Necessary ?? ← Poor response / ↑↑ relapse / Asympt — Tt

1st line

- Antibiotics ← Tetracyclines → مع phototherapy (dev. photo-sensitivity); Erythro (200 mg / 6 hr for 6 ws cases)
- Phototherapy ✓
- Topical CS / Calcineurins → CIs

2nd lines

- MTX, Acitretin, Dapsone
- ulceronecrotic → Wound care.

Cut B-cell Lymphomas (CBCL)

< 1ry cut
2ry Focal

Def: Mg prolif. of cut B Lymphocytes; during different stages of Develop
- represent (20%) of All cut. Lymphomas.

Etiopathogensis: starts as reactive inflammatory process
& in presence of some factors ⟶ (??) Malignant;

1- Immuno deficiency.

2- defective oncogenic Genes.

3- oncogenic organisms:
- (i) Bact < Borrelia / H. pylori (in MZL)
- (ii) Viruses: HHV8, EBV, HCV, HTLV.

سؤال امتحان Q

Epidemiology: - Age, - Sex] → (Elderly ♂ > ♀)

- MR: → in general CBCL has Good prognosis:-

5ys survival Rate is
- FCL & MZL → (≥ 95%)
- DLBCL: (20%) (Intrav.) - (50%) (leg)

Classificat^ of CBCL (WHO-EORTC 2007)

- Follicle Centre (FCL) (2 subtypes <)
- Marginal Zone (MZL) [MAL Type] (2 sub types) →
- Diffuse large (DL) ⟶
  - Leg Type
  - IntraVascular Type
  - other Types: (NOS)
    - Plasmablastic
    - T-Cell / Histiocytes rich.

X

- MZL subtypes:
  - 1r cut. "plasmacytoma"
  - Immunocytoma (Syn: Waldenstrom Macroglob)

- FC subtypes:
  - Reticulohistio-cytoma of Back
  - Cutis Lymphoma

X

Sub Types of (non Dry) IntraVascular
- Lymphomatoid granulomatosis
- Burkitt L.
- Mantle cell L.
- Chr. Lympho-cytic leukemia.

Clinical presentation

- General C/P: From a dermatological point of view, they are characterized by asymptomatic, few, relatively fast growing nodules or infiltrations (plaques) erythematous (may be single)
- General HP: monomorphic (large or small cell), and the neoplastic cell infiltrate is separated from the epidermis by a collagen band (Grenz zone). Rare cases show epidermotropism and can be confused with mycosis fung

Non:
- itchy
- ulcerating
- scalp

(1)

النوع ص site

FCL = center of body

- Head, Neck, Scalp & Trunk (sp. upper back → Crosti type)

prognosis — Excellent (except leg & Foxl1 type)
- rare extracut. spread.
- ~40% recurrence

(++) — few lesions → radiotherapy
Multiples → Combinat° Chemoth.

(2)

Mucosa ass. lymphoid tissue

MZL (MALT)

- UL > L.L & ± Generalized.
- as FCL: excellent prog (5Ys survival rate is > 95%)

(++) — few lesions → radio ± surgical
Multiple: chemoth.

The 2 Types are Indolent ē ← good prognosis.

poor prognosis → **DLBCL** (3)

Leg Type

- Elderly ♀
- Aggressive ē Bad prognosis — 5Ys survival < 50%; Common Extracut. spread.
- (++): . few lesions → Radio.
  . Multiple ll & extracut.: ← Chemoth. ← Rituximab.

Intravascular Type

- Mg B cell infilt. of BVs of skin / CNS
- (No Extravascular Mg cells)
- Skin lesion: as General + Tender & Telangiectatic
- at Trunk & legs
- Poor prognosis ē extracut. spread
- DD ← MF, Vascular Tms, Sarcoidosis

. BVs of skin & CNS
. Tender
. Cutaneous / الجلد

Other Types

- plasmablastic dendritic cell Neoplasm
- rare aggressive Type
- Bruise-like plaques & Nodules ē CNS spread.
- ± Type of Leukemia Cutis.

HP + Immunopheno Typing → Skin Biopsy / LN Biopsy

FCL

Follicular ← تجمع

- Follicular to diffuse dermal infilt by:
  - Centrocytes = (large, cleaved)
  - ± Centroblasts = (large, round)
- Centrocytes (cleaved cells) + Grenz Zone
  - Follicular pattern
  - large cleaved cells

DD: 2ry Cut. Lymphoma:

- Bcl-2 +ve in
- +(14:18) } FCL

MZL

or Marginal Zone ...

- follicular to diffuse dermal & S.C.T infilt

By:

- macrophages → ① Monocytoid cells: (Small Med cells ē indented Nucl & pale cytopl).
- Neutrophils & eosinophils
- ② Lymphoplasmacytoid (Lpc)

NB Inverse pattern ± seen: darker chromatin rich cells surr by pale cells.

DLBCL

Leg Type

→ Diffuse dermal, S.ct & Adnexal infilt by large B-cells called: Centroblasts or Immunoblasts + Grenz Zone.

IntraVascular Type

- as Leg Type but Vascular Infiltrate

.Cleaved: Nuclear Memb. clefts

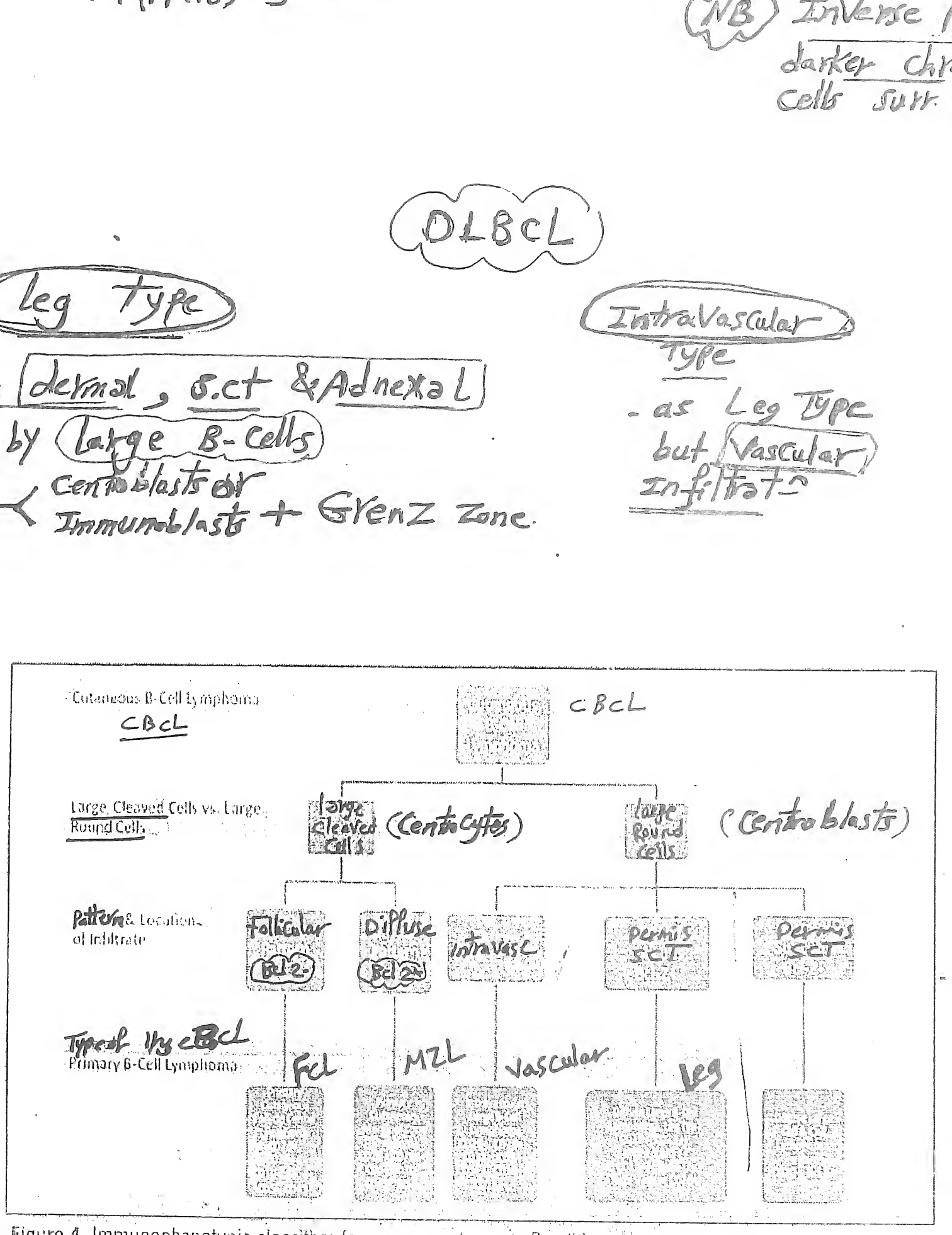


Figure 4. Immunophenotypic algorithm for primary cutaneous B-cell lymphoma